Trimethylsilyl Trifluoromethanesulfonate Catalyzed Nucleophilic Substitution To Give *C*- and *N*-Glucopyranosides Derived from D-Glucopyranose

Yoshiki Oda, Takashi Yamanoi*

The Noguchi Institute, 1-8-1 Kaga, Itabashi-ku, Tokyo 173-0003, Japan
E-mail: tyama@noguchi.or.jp

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Abstract: This paper describes the synthesis of *C*- and *N*-glucopyranosides via trimethylsilyl trifluoromethanesulfonate catalyzed nucleophilic substitution of glucopyranosides, derived from D-glucopyranose, with methyl, ethyl, *n*-butyl, allyl, benzyl, and phenyl groups at the anomeric carbon centers. Generally, the reactions using allyltrimethylsilane, trimethylsilyl azide, trimethylsilyl cyanide, and 1-phenyl-1-(trimethylsiloxy)ethene as the nucleophiles in the presence of 20 mol% trimethylsilyl trifluoromethanesulfonate in acetonitrile at –40 °C smoothly proceeded with α-stereoselectivity to afford various *C*- and *N*-glucopyranosides in 78–99% yield. Although a decrease in the synthetic yields was observed for some reactions using glucopyranoses with allyl and benzyl groups at the anomeric carbon, the yields could be improved using glucopyranosyl acetates in the presence of 20 mol% trimethylsilyl trifluoromethanesulfonate in acetonitrile–dichloromethane (1:1) at –78 °C.

Key words: glycosides, nucleophilic substitutions, D-glucopyranose, trifluoromethanesulfonate catalysis, trimethylsilylated nucleophiles

The study of glycosides has become very significant in the fields of carbohydrate chemistry and biochemistry.[1] Glycosides containing a *C*-glycosidic bond exist in some subunits of naturally occurring products, and are also potentially useful as chiral intermediates in organic chemistry.[2] Therefore, considerable effort is currently devoted to the development of effective synthetic methods for *C*-glycosides which involve carbon–carbon bond formation at the anomeric centers of the carbohydrates.

The addition of an organometallic reagent (e.g., RLi or RMgX) to sugar lactones readily produces a novel class of various artificial ketoses.[3] The effective C- or O-glycosidations of the artificial ketoses to synthesize biologically and chemically important glycosides have been studied by some research groups.[4]

Our recent studies showed the O-glycosidation of benzyl-protected glucopyranoses, derived from D-glucopyranose, containing different alkyl groups (e.g., methyl, ethyl, *n*-butyl, and benzyl groups) at the anomeric carbon position. We also reported O-glycosidation methods for producing various kinds of glucopyranosides from the corresponding glucopyranose derivatives with dimethylphosphinothioyloxy, acetoxy, or hydroxy functions as the leaving groups in the presence of a Lewis or Brønsted acid.[5] Among these glucopyranose derivatives, the glucopyranosyl acetates, which could be effectively activated by catalytic scandium trifluoromethanesulfonate, worked as highly reactive glucopyranosyl donors.

For C-glycosidation, our preliminary letter described the synthesis of *C*-glucopyranosides by the C-allylation of the corresponding glucopyranoses.[6] The reaction performed with allyltrimethylsilane as nucleophile in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in acetonitrile afforded the C-allylated glucopyranosides. To the best of our knowledge, this is the first synthetic approach to give various kinds of C-allylated glucopyranosides (*C*,*C*-dialkyl-D-glucopyranosides). After our C-allylation method was published, Gomez et al. reported a similar glycosidation of ketoses derived from D-glucopyranose using several C- and N-nucleophiles.[4b]

During our investigation into the C-allylation, we found that glucopyranoses with β,γ-unsaturated allyl or benzyl groups at the anomeric center showed different reactivity from those derivatives containing other alkyl groups.[7] The C-allylation of the allyl or benzyl derivatives did not produce the glucopyranosides in satisfactory yields and byproducts were observed. Therefore, it was necessary to further investigate the glycosidation of these glucopyranoses with various nucleophiles and to develop a more useful C-glycosidation method. Such a development has great significance because it can contribute to the synthesis of various kinds of glucopyranosides, which are not only useful chiral building blocks for constructing natural products, but also attractive precursors for designing and synthesizing novel glycosidase inhibitors.

Therefore, we studied the glycosidation methods for synthesizing various *C*- and *N*-glucopyranosides. In this paper, we describe the C- and N-glycosidations of glucopyranoses, derived from D-glucopyranose, with methyl, ethyl, *n*-butyl, allyl, benzyl, and phenyl groups at the anomeric carbon using several trimethylsilylated nucleophiles in the presence of TMSOTf.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-α-D-glucopyranose (**1a**), 2,3,4,6-tetra-*O*-benzyl-1-*C*-ethyl-α-D-glucopyranose (**1b**),[8] 2,3,4,6-tetra-*O*-benzyl-1-*C*-*n*-butyl-α-D-glucopyranose (**1c**), 1-*C*-allyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1d**),[9] 1-*C*-benzyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1e**),[9] and 2,3,4,6-tetra-*O*-benzyl-1-*C*-phenyl-α-D-glucopyranose (**1f**)[10] were used as the D-glucopyranose derivatives (Figure 1). The glucopyranoses could be prepared in 86–98% yield by the addition of the

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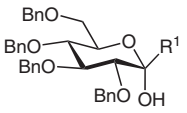
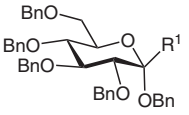
organometallic reagent (RLi or RMgX) to 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone.



R^1 = Me; **1a**
Et; **1b**
n-Bu; **1c**
All; **1d**
Bn; **1e**
Ph; **1f**

Figure 1

As previously reported, the C-allylation of **1a** with allyltrimethylsilane in the presence of TMSOTf produced benzyl 2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-α-D-glucopyranoside (**2a**)[11] (Figure 2) as a major byproduct along with the desired C-allylated glucopyranoside **3a** (Scheme 1). This was attributed to benzyl alcohol, produced with the degradation of **1a** under the given reaction conditions, acting as a glycosyl acceptor of **1a** to afford the glycoside **2a**. Therefore, we investigated the effects of different solvents, temperatures, and amounts of reagents on the C-allylation reaction using **1a** in the presence of the drying agent, calcium sulfate. We found that the reaction conditions using three equivalents of allyltrimethylsilane in acetonitrile at –40 °C in the presence of 20 mol% TMSOTf smoothly produced **3a** in 88% yield with almost no formation of **2a** (Table 1, entry 7). The reaction conditions were also effective for the C-allylation of **1b**, **1c**, and **1f**, containing normal alkyl and phenyl groups at the anomeric center, to afford the C-allylated glucopyranosides **3b**, **3c**, and **3f** in 88–95% yield (entries 8, 9, and 12, respectively). Under the same reaction conditions, however, glucopyranoses **1d** and **1e** did not produce the corresponding *C*-glucopyranosides **3d** and **3e** in satisfactory yields and the benzyl glycosides **4d** and **4e** (Figure 2), respectively, were still produced as major byproducts. It appeared that the electronic or steric effects of the functional groups at the anomeric centers of **1d** and **1e** influenced the leaving ability of the hemiacetal hydroxy group and the production of **4d** and **4e**.



R^1 = Me; **2a**
All; **4d**
Bn; **4e**

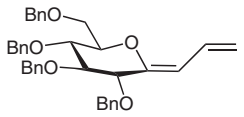


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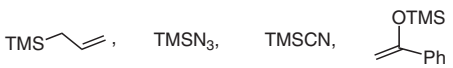
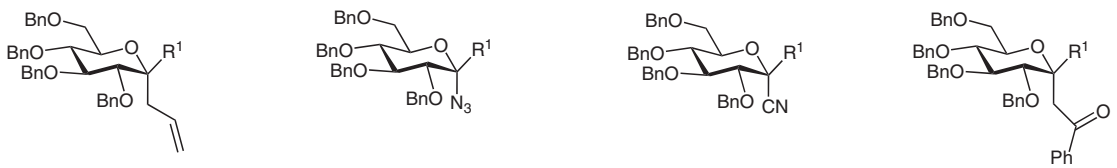
Figure 2

We then investigated the reactions of glucopyranoses **1a–f** with various kinds of trimethylsilylated nucleophiles, i.e. trimethylsilyl azide, trimethylsilyl cyanide, and 1-phenyl-1-(trimethylsiloxy)ethene, under similar reaction conditions in order to demonstrate the synthesis of various kinds of *C*- and *N*-glucopyranosides (Scheme 1, Table 1). All the reactions of **1a–c** and **1f** with these nucleophiles (3

C- or N-nucleophile = 

glucopyranoside = 

R^1 = Me; **3a**
Et; **3b**
n-Bu; **3c**
All; **3d**
Bn; **3e**
Ph; **3f**

R^1 = Me; **5a**
Et; **5b**
n-Bu; **5c**
All; **5d**
Bn; **5e**
Ph; **5f**

R^1 = Me; **6a**
Et; **6b**
n-Bu; **6c**
All; **6d**
Bn; **6e**

R^1 = Me; **7a**
Et; **7b**
n-Bu; **7c**
All; **7d**
Bn; **7e**
Ph; **7f**

Scheme 1

equiv) in acetonitrile at –40 °C in the presence of 20 mol% TMSOTf successfully produced the desired glucopyranosides (i.e., **5a–c** and **5f**, **6a–c**, and **7a–c** and **7f**) in 78–99% yields. For the corresponding reactions of **1d** and **1e**, using trimethylsilyl azide afforded **5d** and **5e** both in 80% yield, while the reactions using trimethylsilyl cyanide and 1-phenyl-1-(trimethylsiloxy)ethene gave **6d** and **6e** and **7d** and **7e**, respectively, in 53–73% yields. The differences in the nucleophilic species significantly influenced the yields of these glucopyranosides. In general, the yields of the *C*- and *N*-glucopyranosides were lower for the reactions using **1d** and **1e** than for those using **1a–c** and **1f**. This was a similar result to that obtained for the reactions using allyltrimethylsilane, as mentioned above.

Table 1 Reactions of Glucopyranoses **1** or Glucopyranosyl Acetates **9** with Various C- or N-Nucleophiles in the Presence of Trimethylsilyl Trifluoromethanesulfonate

Entry[a]	Substrate	Nucleophile	Solvent	Temp (°C)	Product	Yield (%)
1[b]	**1a**	$TMSCH_2CH=CH_2$	CH_2Cl_2	–10	**3a**	49 (30)[c]
2[b]	**1a**	$TMSCH_2CH=CH_2$	Et_2O	–10	**3a**	trace (25)[c]
3[b]	**1a**	$TMSCH_2CH=CH_2$	MeCN	–10	**3a**	67 (15)[c]
4[d]	**1a**	$TMSCH_2CH=CH_2$	MeCN	–10	**3a**	76 (9)[c]
5[d]	**1a**	$TMSCH_2CH=CH_2$	MeCN	–20	**3a**	79 (7)[c]
6[d]	**1a**	$TMSCH_2CH=CH_2$	MeCN	–40	**3a**	84 (3)[c]
7	**1a**	$TMSCH_2CH=CH_2$	MeCN	–40	**3a**	88
8	**1b**	$TMSCH_2CH=CH_2$	MeCN	–40	**3b**	88
9	**1c**	$TMSCH_2CH=CH_2$	MeCN	–40	**3c**	88
10	**1d**	$TMSCH_2CH=CH_2$	MeCN	–40	**3d**	31 (17)[e]
11	**1e**	$TMSCH_2CH=CH_2$	MeCN	–40	**3e**	18
12	**1f**	$TMSCH_2CH=CH_2$	MeCN	–40	**3f**	95
13[f]	**1d**	$TMSCH_2CH=CH_2$	MeCN–CH_2Cl_2 (1:1)	–78	**3d**	53 (16)[g]
14[h]	**1e**	$TMSCH_2CH=CH_2$	MeCN–CH_2Cl_2 (1:1)	–78	**3e**	78
15	**1a**	$TMSN_3$	MeCN	–40	**5a**	99
16	**1b**	$TMSN_3$	MeCN	–40	**5b**	96
17	**1c**	$TMSN_3$	MeCN	–40	**5c**	94
18	**1d**	$TMSN_3$	MeCN	–40	**5d**	80
19	**1e**	$TMSN_3$	MeCN	–40	**5e**	80
20	**1f**	$TMSN_3$	MeCN	–40	**5f**	96
21	**1a**	TMSCN	MeCN	–40	**6a**	95
22	**1b**	TMSCN	MeCN	–40	**6b**	90
23	**1c**	TMSCN	MeCN	–40	**6c**	92
24	**1d**	TMSCN	MeCN	–40	**6d**	65
25	**1e**	TMSCN	MeCN	–40	**6e**	73
26	**1a**	$H_2C=C(OTMS)Ph$	MeCN	–40	**7a**	98
27	**1b**	$H_2C=C(OTMS)Ph$	MeCN	–40	**7b**	91
28	**1c**	$H_2C=C(OTMS)Ph$	MeCN	–40	**7c**	87
29	**1d**	$H_2C=C(OTMS)Ph$	MeCN	–40	**7d**	53
30	**1e**	$H_2C=C(OTMS)Ph$	MeCN	–40	**7e**	61

Table 1 Reactions of Glucopyranoses **1** or Glucopyranosyl Acetates **9** with Various C- or N-Nucleophiles in the Presence of Trimethylsilyl Trifluoromethanesulfonate (continued)

Entry[a]	Substrate	Nucleophile	Solvent	Temp (°C)	Product	Yield (%)
31	**1f**	H_2C=C(OTMS)Ph	MeCN	–40	**7f**	78
32	**9e**	$TMSCH_2CH$=CH_2	MeCN	–40	**3e**	66 (10)[i]
33	**9e**	$TMSCH_2CH$=CH_2	MeCN–CH_2Cl_2 (1:1)	–78	**3e**	80
34	**9d**	$TMSCH_2CH$=CH_2	MeCN–CH_2Cl_2 (1:1)	–78	**3d**	72
35	**9d**	$TMSN_3$	MeCN–CH_2Cl_2 (1:1)	–78	**5d**	94
36	**9e**	$TMSN_3$	MeCN–CH_2Cl_2 (1:1)	–78	**5e**	91
37	**9d**	TMSCN	MeCN–CH_2Cl_2 (1:1)	–78	**6d**	95
38	**9e**	TMSCN	MeCN–CH_2Cl_2 (1:1)	–78	**6e**	86
39	**9d**	H_2C=C(OTMS)Ph	MeCN–CH_2Cl_2 (1:1)	–78	**7d**	93
40	**9e**	H_2C=C(OTMS)Ph	MeCN–CH_2Cl_2 (1:1)	–78	**7e**	91

[a] Conditions: molar ratio (glucopyranose derivative/nucleophile/TMSOTf) 1:3:0.2, 2–3 h.
[b] Molar ratio (glucopyranose/allyltrimethylsilane/TMSOTf) 1:2:0.1.
[c] The yield in parenthesis is that of byproduct **2a**.
[d] Molar ratio (glucopyranose/allyltrimethylsilane/TMSOTf) 1:2:0.2.
[e] The yield in parenthesis is that of byproduct **4d**.
[f] Molar ratio (glucopyranose/allyltrimethylsilane/TMSOTf) 1:6:0.2.
[g] The yield in parenthesis is that of byproduct **8**.
[h] Molar ratio (glucopyranose/allyltrimethylsilane/TMSOTf) 1:6:0.4.
[i] The yield in parenthesis is that of byproduct **4e**.

Our next effort was directed at improving in the yields for the reactions of **1d** and **1e** with allyltrimethylsilane (Scheme 1). First, we attempted changing the reaction temperatures and amounts of the reagents. Although for the reactions using excess amounts of the reagents, the yields of **3d** and **3e** increased to 53 and 78% (Table 1, entries 13 and 14), respectively, they were not satisfactory yields. In addition, the production of *exo*-glycal derivative **8**[9] as a novel byproduct was observed in 16% yield for the reaction of **1d** (Figure 2).

In order to increase the reactivities of **1d** and **1e**, we transformed them into the corresponding glucopyranosyl acetates. Acetates **9d** and **9e**[4c,d] were obtained in 82 and 94% yield, respectively, from the reactions of **1d** and **1e** with acetic anhydride using *n*-butyllithium in tetrahydrofuran. Compounds **9d** and **9e** were expected to be highly reactive as glycosyl donors based on our findings that glucopyranose derivatives with an acetoxy leaving group were good glycosyl donors in our O-glycosidation method. The C-allylation of **9e** with allyltrimethylsilane in the presence of 20 mol% TMSOTf in acetonitrile at –40 °C afforded **3e** in 66% yield (Table 1, entry 32), and the reaction in acetonitrile–dichloromethane (1:1) at –78 °C successfully gave **3e** in good yield (80%, entry 33). Under similar conditions using the latter solvent mixture, all the reactions of **9d** and **9e** with allyltrimethylsilane, trimethylsilyl azide, trimethylsilyl cyanide, and 1-phenyl-1-(trimethylsiloxy)ethene produced the corresponding glucopyranosides **3d** and **3e**, **5d** and **5e**, **6d** and **6e**, and **7d** and **7e** in excellent yields (entries 33–40) (Scheme 1).

All the glucopyranosides were produced as single isomers, and their NMR spectra indicated that there were nuclear Overhauser effect (NOE) interactions between the H-1′ (or aromatic H) and H-3 protons as shown in Figure 3. These observations indicated that the nucleophilic attack took place stereoselectively at the α-side of the oxocarbenium cation intermediates generated from **1a**–**f**. The axial attack was advantageous for the direct formation of the chair conformation from the oxocarbenium cation intermediates, and it forced the original anomeric functional groups of **1a**–**f** to take an equatorial orientation, which would contribute to the stabilization of the $^4C_1$ conformation (Scheme 2).

In summary, we have investigated the synthesis of various kinds of *C*- and *N*-glucopyranosides by TMSOTf-cata-

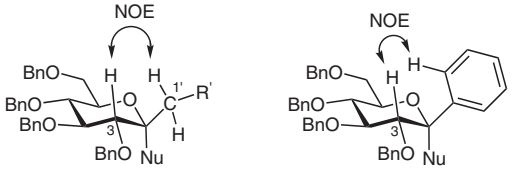
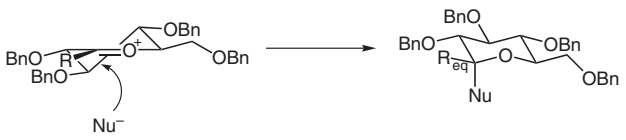


Figure 3



Scheme 2

lyzed nucleophilic substitutions to glucopyranoses **1a–f** using several trimethylsilylated nucleophiles. Generally, the C- and N-glycosidations performed in the presence of 20 mol% TMSOTf in acetonitrile at –40 °C proceeded smoothly with α-stereoselectivity to afford the glucopyranosides in excellent yields. For those reactions using **1d** and **1e**, the yields of the produced glucopyranosides decreased. The yields of these glucopyranosides were remarkably improved by using glucopyranosyl acetates **9d** and **9e** as the substrates in the presence of 20 mol% TMSOTf in acetonitrile–dichloromethane (1:1) at –78 °C.

^{1}H and ^{13}C NMR spectra were recorded on JEOL EX-400 and ECA-600 spectrometers (JEOL) in $CDCl_3$ using TMS as the internal standard. Optical rotations were recorded on a JASCO DIP-360 digital polarimeter. HRMS were obtained using a Mariner spectrometer (PerSeptive Biosystems Inc.). Preparative TLC was performed on Merck silica gel 60GF254. Column chromatography was conducted using silica gel 60N (40–50 μm, Kanto Chemical Co., Inc.) All dry solvents were purified according to the standard methods. The spectral data of **2a**, **3a**, **5a**, **6a**, **7a** and **8a** are reported in the literature.[4b,9,11]

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran (3a) (Table 1, Entry 7)

TMSOTf (7.2 μL, 0.04 mmol) was added to a solution of **1a** (110.0 mg, 0.2 mmol) and allyltrimethylsilane (94.7 μL, 0.6 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h. The reaction was then quenched by the addition of sat. $NaHCO_3$ soln (5 mL). The mixture was extracted with $CHCl_3$, and the organic layer was washed with H_2O and sat. NaCl soln. After the organic layer was dried (Na_2SO_4), the solvent was evaporated under reduced pressure. The crude product was purified by preparative TLC (silica gel, EtOAc–hexane, 1:4) to give **3a**[4b] as a white oil. Yield: 101 mg (88%).

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran (3a) and (2*S*,3*R*,4*S*,5*R*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran (2a) (Table 1, Entry 4)

TMSOTf (7.2 μL, 0.04 mmol) was added to a solution of **1a** (110.9 mg, 0.2 mmol) and allyltrimethylsilane (63.5 μL, 0.4 mmol) in MeCN (3 mL) at –10 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**. The crude mixture was separated by preparative TLC (silica gel, EtOAc–hexane, 1:4) to give **3a** and **2a**[11] as white oils; Yield of **3a**: 88.2 mg (76%); yield of **2a**: 11.8 mg (9%).

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-ethyltetrahydropyran (3b) (Table 1, Entry 8)

TMSOTf (7.3 μL, 0.04 mmol) was added to a solution of **1b** (113.2 mg, 0.2 mmol) and allyltrimethylsilane (94.9 μL, 0.6 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3b** as a white oil. Yield: 104.4 mg (88%).

$[\alpha]_D^{23}$ +47.3 (*c* 4.31, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.52–1.61 (m, 1 H, $CH_aH_bCH_3$), 1.76–1.85 (m, 1 H, $CH_aH_bCH_3$), 2.38 (dd, *J* = 7.8, 15.4 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 2.69 (dd, *J* = 6.3, 15.4 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 3.59 (d, *J* = 9.5 Hz, 1 H, H-3), 3.60 (t, *J* = 9.5 Hz, 1 H, H-5), 3.64–3.67 (m, 1 H, H-6), 3.68–3.69 (m, 1 H, H_a-7), 3.75 (dd, *J* = 4.2, 11.2 Hz, 1 H, H_b-7), 3.93 (t, *J* = 9.5 Hz, 1 H, H-4), 4.53–4.93 (m, 8 H, CH_2Ph), 5.08–5.12 (m, 2 H, $CH_2CH{=}CH_2$), 5.80–5.91 (m, 1 H, $CH_2CH{=}CH_2$), 7.19–7.35 (m, 20 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.2 (CH_2CH_3), 28.5 (CH_2CH_3), 34.8 ($CH_2CH{=}CH_2$), 69.4 (C-7), 72.4 (C-6), 73.3 (CH_2Ph), 75.0 (CH_2Ph), 75.6 (2 CH_2Ph), 78.1 (C-2), 79.2 (C-5), 80.7 (C-3), 84.4 (C-4), 117.7 ($CH_2CH{=}CH_2$), 127.3–128.3 (Ph), 133.0 ($CH_2CH{=}CH_2$), 138.1–138.5 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{39}H_{44}O_5$: 615.3086; found: 615.3081.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-butyltetrahydropyran (3c) (Table 1, Entry 9)

TMSOTf (6.9 μL, 0.038 mmol) was added to a solution of **1c** (112.7 mg, 0.19 mmol) and allyltrimethylsilane (94.9 μL, 0.6 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3c** as a white oil. Yield: 103.2 mg (88%).

$[\alpha]_D^{23}$ +32.1 (*c* 5.16, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.17–1.29 (m, 3 H, $CH_2CH_aH_bCH_2CH_3$), 1.50–1.57 (m, 2 H, $CH_aH_bCH_aH_bCH_2CH_3$), 1.67–1.72 (m, 1 H, $CH_aH_bCH_2CH_2CH_3$), 2.37 (dd, *J* = 7.8, 15.4 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 2.68 (dd, *J* = 6.3, 15.4 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 3.59 (t, *J* = 9.3 Hz, 1 H, H-5), 3.60 (d, *J* = 9.3 Hz, 1 H, H-3), 3.63–3.65 (m, 1 H, H-6), 3.65–3.68 (m, 1 H, H_a-7), 3.74 (dd, *J* = 4.1, 11.1 Hz, 1 H, H_b-7), 3.92 (t, *J* = 9.0 Hz, 1 H, H-4), 4.53–4.92 (m, 8 H, CH_2Ph), 5.08–5.12 (m, 2 H, $CH_2CH{=}CH_2$), 5.81–5.91 (m, 1 H, $CH_2CH{=}CH_2$), 7.18–7.36 (m, 20 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 ($CH_2CH_2CH_2CH_3$), 23.2 ($CH_2CH_2CH_2CH_3$), 25.0 ($CH_2CH_2CH_2CH_3$), 34.8 ($CH_2CH{=}CH_2$), 35.8 ($CH_2CH_2CH_2CH_3$), 69.3 (C-7), 72.4 (C-6), 73.2 (CH_2Ph), 75.0 (CH_2Ph), 75.1 (CH_2Ph), 75.5 (CH_2Ph), 78.2 (C-2), 79.2 (C-5), 81.3 (C-3), 84.5 (C-4), 117.7 ($CH_2CH{=}CH_2$), 127.3–128.3 (Ph), 133.0 ($CH_2CH{=}CH_2$), 138.1–138.5 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{41}H_{48}O_5$: 643.3399; found: 643.3416.

(3*R*,4*S*,5*R*,6*R*)-2,2-Diallyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3d) (Table 1, Entry 34)

TMSOTf (8.4 μL, 0.046 mmol) was added to a solution of **9d** (143.5 mg, 0.23 mmol) and allyltrimethylsilane (220 μL, 1.38 mmol) in MeCN–CH_2Cl_2 (1:1, 3 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3d** as a white oil. Yield: 139.4 mg (72%).

$[\alpha]_D^{23}$ +72.6 (*c* 1.90, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (dd, *J* = 9.4, 14.8 Hz, 1 H, β-$CH_aH_bCH{=}CH_2$), 2.31 (dd, *J* = 8.1, 15.4 Hz, 1 H, α-$CH_aH_bCH{=}CH_2$), 2.51 (dd, *J* = 4.6, 14.6 Hz, 1 H, β-$CH_aH_bCH{=}CH_2$), 2.63 (dd, *J* = 6.1, 15.4 Hz, 1 H, α-$CH_aH_bCH{=}CH_2$), 3.50 (t, *J* = 9.5 Hz, 1 H, H-5), 3.53 (d, *J* = 9.5 Hz, 1 H, H-3), 3.57–3.61 (m, 1 H, H-6), 3.62–3.69 (m, 2 H, H-7), 3.83 (t, *J* = 9.3 Hz, 1 H, H-4), 4.47–4.84 (m, 8 H, CH_2Ph), 4.94–5.06 (m, 4 H, $CH_2CH{=}CH_2$), 5.74–5.94 (m, 2 H, $CH_2CH{=}CH_2$), 7.20–7.34 (m, 20 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.3 (α-$CH_2CH{=}CH_2$), 40.7 (β-$CH_2CH{=}CH_2$), 69.3 (C-7), 72.6 (C-6), 73.3 (CH_2Ph), 74.7 (CH_2Ph), 75.1 (CH_2Ph), 75.5 (CH_2Ph), 78.7 (C-2), 79.1 (C-5), 81.3 (C-3), 84.4 (C-4), 117.9 (α-$CH_2CH{=}CH_2$), 118.1 (β-$CH_2CH{=}CH_2$), 127.0–128.3 (Ph), 132.5 (α-$CH_2CH{=}CH_2$), 134.4 (β-$CH_2CH{=}CH_2$), 138.0–138.8 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{40}H_{44}O_5$: 627.3086; found: 627.3031.

(3*R*,4*S*,5*R*,6*R*)-2,2-Diallyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3d) and (2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2,3,4,5-tetrakis(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (4d) (Table 1, Entry 10)

TMSOTf (7.2 μL, 0.04 mmol) was added to a solution of **1d** (114.9 mg, 0.2 mmol) and allyltrimethylsilane (94.3 μL, 0.59 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**. The crude mixture was separated by preparative TLC (silica gel, EtOAc–hexane 1:4) to give **3d** and **4d** as white oils. Yield of **3d**: 37.3 mg (31%); yield of **4d**: 22.3 mg (17%).

4d

$[\alpha]_D^{23}$ +66.7 (*c* 0.3, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.65 (dd, *J* = 9.0, 13.7 Hz, 1 H, C$H_a$$H_b$CH=$CH_2$), 2.69–2.73 (m, 1 H, CH_aH_bCH=CH_2), 3.56 (d, *J* = 9.6 Hz, 1 H, H-3), 3.61 (t, *J* = 9.6 Hz, 1 H, H-5), 3.67 (d, *J* = 11.0 Hz, 1 H, H_a-7), 3.74 (dd, *J* = 4.1, 11.0 Hz, 1 H, H_b-7), 3.77–3.79 (m, 1 H, H-6), 4.13 (t, *J* = 9.6 Hz, 1 H, H-4), 4.52–4.96 (m, 10 H, CH_2Ph), 5.01–5.07 (m, 2 H, CH_2CH=CH_2), 5.83–5.90 (m, 1 H, CH_2C*H*=CH_2), 7.08–7.47 (m, 25 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 38.3 (*C*H_2CH=CH_2), 62.3 (*C*H_2Ph), 68.9 (C-7), 72.1 (C-6), 73.3 (*C*H_2Ph), 74.7 (*C*H_2Ph), 75.0 (*C*H_2Ph), 75.4 (*C*H_2Ph), 78.8 (C-5), 81.3 (C-3), 83.4 (C-4), 102.1 (C-2), 118.1 (CH_2CH=*C*H_2), 127.0–128.3 (Ph), 133.6 (CH_2*C*H=CH_2), 138.2–138.9 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{44}H_{46}O_6$: 693.3192; found: 693.3167.

(3*R*,4*S*,5*R*,6*R*)-2,2-Diallyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3d) and (*Z*)-(3*R*,4*S*,5*R*,6*R*)-2-Allylidene-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (8) (Table 1, Entry 13)

TMSOTf (7.5 μL, 0.041 mmol) was added to a solution of **1d** (119.9 mg, 0.21 mmol) and allyltrimethylsilane (196.9 μL, 1.24 mmol) in MeCN–CH_2Cl_2 (1:1, 3 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**. The crude mixture was separated by preparative TLC (silica gel, EtOAc–hexane 1:4) to give **3d** and **8**[9] as white oils. Yield of **3d**: (66.3 mg, 53%); yield of **8**: 18.2 mg (16%).

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3e) (Table 1, Entry 14)

TMSOTf (14.8 μL, 0.081 mmol) was added to a solution of **1e** (128.5 mg, 0.20 mmol) and allyltrimethylsilane (194.2 μL, 1.22 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3e** as a white oil. Yield: 103.5 mg (78%).

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3e) (Table 1, Entry 33)

TMSOTf (4.5 μL, 0.024 mmol) was added to a solution of **9e** (83.7 mg, 0.12 mmol) and allyltrimethylsilane (59.3 μL, 0.37 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3e** as a white oil. Yield: 64.8 mg (80%).

$[\alpha]_D^{23}$ +27.4 (*c* 5.18, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (dd, *J* = 8.0, 15.3 Hz, 1 H, C$H_a$$H_b$CH=$CH_2$), 2.79 (d, *J* = 14.4 Hz, 1 H, CC$H_a$$H_b$Ph), 2.81 (dd, *J* = 7.3, 14.8 Hz, 1 H, CH_aH_bCH=CH_2), 3.19 (d, *J* = 14.4 Hz, 1 H, CCH_aH_bPh), 3.35 (d, *J* = 9.5 Hz, 1 H, H-3), 3.49 (t, *J* = 9.5 Hz, 1 H, H-5), 3.68–3.74 (m, 1 H, H-6), 3.75–3.82 (m, 2 H, H-7), 3.92 (t, 1 H, *J* = 9.2 Hz, H-4), 4.22–4.90 (m, 8 H, CH_2Ph), 5.15–5.19 (m, 2 H, CH_2CH=CH_2), 5.90–5.98 (m, 1 H, CH_2C*H*=CH_2), 7.13–7.37 (m, 25 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.1 (*C*H_2CH=CH_2), 42.3 (C*C*H_2Ph), 69.5 (C-7), 72.5 (C-6), 73.3 (*C*H_2Ph), 74.3 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.6 (*C*H_2Ph), 79.0 (C-5), 79.5 (C-2), 80.3 (C-3), 84.7 (C-4), 118.1 (CH_2CH=*C*H_2), 126.1–131.1 (Ph), 132.7 (CH_2*C*H=CH_2), 137.4–139.1 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{44}H_{46}O_5$: 677.3237; found: 677.3176.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (3e) and (2*S*,3*R*,4*S*,5*R*,6*R*)-2-Benzyl-2,3,4,5-tetrakis(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (4e) (Table 1, Entry 32)

TMSOTf (5.0 μL, 0.027 mmol) was added to a solution of **9e** (91.8 mg, 0.14 mmol) and allyltrimethylsilane (65 μL, 0.41 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**. The crude mixture was separated by preparative TLC (silica gel, EtOAc–hexane, 1:4) to give **3e** and **4e** as white oils. Yield of **3e**: 59.3 mg (66%); yield of **4e**: 10 mg (10%).

4e

$[\alpha]_D^{23}$ +48.7 (*c* 1.03, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.05 (d, *J* = 13.8 Hz, 1 H, CC$H_a$$H_b$Ph), 3.24 (d, *J* = 9.0 Hz, 1 H, H-3), 3.29 (d, *J* = 13.8 Hz, 1 H, CCH_aH_bPh), 3.47 (t, *J* = 9.6 Hz, 1 H, H-5), 3.68–3.76 (m, 3 H, H-6, H-7), 4.10 (t, *J* = 9.6 Hz, 1 H, H-4), 4.32–4.85 (m, 8 H, CH_2Ph), 7.13–7.37 (m, 30 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 40.0 (C*C*H_2Ph), 62.3 (O*C*H_2Ph), 69.1 (C-7), 72.2 (C-6), 73.2 (*C*H_2Ph), 74.0 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.4 (*C*H_2Ph), 78.7 (C-5), 80.0 (C-3), 83.5 (C-4), 102.9 (C-2), 126.9–130.5 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{48}H_{48}O_6$: 743.3349; found: 743.3385.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-phenyltetrahydropyran (3f) (Table 1, Entry 12)

TMSOTf (8.1 μL, 0.044 mmol) was added to a solution of **1f** (136.6 mg, 0.22 mmol) and allyltrimethylsilane (105.6 μL, 0.66 mmol) in MeCN (3.0 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **3f** as a white oil. Yield: 134.1 mg (95%).

$[\alpha]_D^{23}$ +12.4 (*c* 6.31, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.92 (dd, *J* = 7.6, 16.5 Hz, 1 H, C$H_a$$H_b$CH=$CH_2$), 3.19 (dd, *J* = 6.2, 16.5 Hz, 1 H, CH_aH_bCH=CH_2), 3.41 (d, *J* = 9.6 Hz, 1 H, H-3), 3.77 (d, *J* = 11.0 Hz, 1 H, H_a-7), 3.82–3.86 (m, 3 H, H-5, H-6, C$H_a$$H_b$Ph), 3.88 (dd, *J* = 2.8, 10.3 Hz, 1 H, H_b-7), 3.98–4.01 (m, 1 H, H-4), 4.54–4.91 (m, 7 H, CH_2Ph, CH_aH_bPh), 4.96 (d, *J* = 10.3 Hz, 1 H, CH_2CH=C$H_a$$H_b$), 5.08 (d, *J* = 17.2 Hz, 1 H, CH_2CH=CH_aH_b), 5.50–5.67 (m, 1 H, CH_2C*H*=CH_2), 7.14–7.40 (m, 23 H, Ph), 7.65 (d, *J* = 7.5Hz, 2 H, CPh).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 31.9 (*C*H_2CH=CH_2), 69.5 (C-7), 72.3 (C-6), 73.4 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.5 (2 *C*H_2Ph), 79.0 (C-5), 79.8 (C-2), 84.2 (C-4), 86.8 (C-3), 117.7 (CH_2CH=*C*H_2), 126.5–128.4 (Ph), 132.6 (CH_2*C*H=CH_2), 138.2–143.2 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{43}H_{44}O_5$: 663.3081; found: 663.3128.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran (5a) (Table 1, Entry 15)

TMSOTf (9.3 μL, 0.051 mmol) was added to a solution of **1a** (141.6 mg, 0.26 mmol) and $TMSN_3$ (101.7 μL, 0.77 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5a**[4b] as a white oil. Yield: 147.1 mg (99%).

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-ethyltetrahydropyran (5b) (Table 1, Entry 16)

TMSOTf (7.6 μL, 0.042 mmol) was added to a solution of **1b** (118.4 mg, 0.21 mmol) and $TMSN_3$ (82.9 μL, 0.62 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5b** as a white oil. Yield: 119.1 mg (96%).

$[\alpha]_D^{23}$ +58.9 (*c* 5.96, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.86–1.91 (m, 1 H, $CH_aH_bCH_3$), 2.03–2.08 (m, 1 H, $CH_aH_bCH_3$), 3.49 (d, *J* = 9.3 Hz, 1 H, H-3), 3.64–3.69 (m, 2 H, H-5, H_a-7), 3.76 (dd, *J* = 3.5, 14.9 Hz, 1 H, H_b-7), 3.85–3.87 (m, 1 H, H-6), 4.00 (t, *J* = 9.3 Hz, 1 H, H-4), 4.49–4.93 (m, 8 H, CH_2Ph), 7.19–7.32 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 7.3 (CH_2CH_3), 28.4 (CH_2CH_3), 68.4 (C-7), 73.3 (CH_2Ph), 73.5 (C-6), 74.9 (CH_2Ph), 75.3 (CH_2Ph), 75.7 (CH_2Ph), 77.7 (C-5), 81.3 (C-3), 83.7 (C-4), 94.3 (C-2), 127.4–138.3 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{36}H_{39}N_3O_5$: 616.2787; found: 616.2749.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-butyltetrahydropyran (5c) (Table 1, Entry 17)

TMSOTf (3.3 μL, 0.018 mmol) was added to a solution of **1c** (53.6 mg, 0.09 mmol) and $TMSN_3$ (35.8 μL, 0.27 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5c** as a white oil. Yield: 52.6 mg (94%).

$[\alpha]_D^{23}$ +52.5 (*c* 2.63, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.22–1.54 (m, 4 H, $CH_2CH_2CH_2CH_3$), 1.78–1.93 (m, 2 H, $CH_2CH_2CH_2CH_3$), 3.49 (d, *J* = 9.2 Hz, 1 H, H-3), 3.63–3.67 (m, 2 H, H-5, H_a-7), 3.75 (dd, *J* = 3.7, 11.1 Hz, 1 H, H_b-7), 3.84–3.86 (m, 1 H, H-6), 3.99 (t, *J* = 9.2 Hz, 1 H, H-4), 4.51–4.94 (m, 8 H, CH_2Ph), 7.19–7.33 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1 ($CH_2CH_2CH_2CH_3$), 22.7 ($CH_2CH_2CH_2CH_3$), 25.0 ($CH_2CH_2CH_2CH_3$), 35.1 ($CH_2CH_2CH_2CH_3$), 68.4 (C-7), 73.2 (CH_2Ph), 73.5 (C-6), 75.0 (CH_2Ph), 75.3 (CH_2Ph), 75.7 (CH_2Ph), 77.8 (C-5), 81.4 (C-3), 83.8 (C-4), 94.2 (C-2), 127.5–138.3 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{38}H_{43}N_3O_5$: 644.3100; found: 644.3062.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2-azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (5d) (Table 1, Entry 18)

TMSOTf (5.3 μL, 0.029 mmol) was added to a solution of **1d** (84.9 mg, 0.15 mmol) and $TMSN_3$ (58.2 μL, 0.44 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5d** as a white oil. Yield: 71.3 mg (80%).

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-2-azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (5d) (Table 1, Entry 35)

TMSOTf (4.7 μL, 0.026 mmol) was added to a solution of **9d** (80.3 mg, 0.13 mmol) and $TMSN_3$ (51.3 μL, 0.39 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5d** as a white oil. Yield: 73.1 mg (94%).

$[\alpha]_D^{23}$ +68.8 (*c* 3.3, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.69 (dd, *J* = 7.8, 14.4 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 2.78 (dd, *J* = 6.1, 14.2 Hz, 1 H, $CH_aH_bCH{=}CH_2$), 3.52 (d, *J* = 9.2 Hz, 1 H, H-3), 3.64–3.69 (m, 2 H, H-5, H_a-7), 3.78 (dd, *J* = 3.6, 11.2 Hz, 1 H, H_b-7), 3.87–3.89 (m, 1 H, H-6), 3.98 (t, *J* = 9.3 Hz, 1 H, H-4), 4.51–4.94 (m, 8 H, CH_2Ph), 5.16 (t, *J* = 17.1 Hz, 2 H, $CH_2CH{=}CH_2$), 5.85–5.88 (m, 1 H, $CH_2CH{=}CH_2$), 7.19–7.35 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 40.0 ($CH_2CH{=}CH_2$), 68.4 (C-7), 73.3 (CH_2Ph), 73.8 (C-6), 75.0 (CH_2Ph), 75.3 (CH_2Ph), 75.7 (CH_2Ph), 77.7 (C-5), 81.4 (C-3), 83.7 (C-4), 93.7 (C-2), 119.7 ($CH_2CH{=}CH_2$), 127.5–128.4 (Ph), 131.3 ($CH_2CH{=}CH_2$), 138.0–138.4 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{37}H_{39}N_3O_5$: 628.2787; found: 628.2737.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (5e) (Table 1, Entry 19)

TMSOTf (4.2 μL, 0.023 mmol) was added to a solution of **1e** (72.2 mg, 0.11 mmol) and $TMSN_3$ (45.6 μL, 0.34 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5e** as a white oil. Yield: 60.9 mg (80%).

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (5e) (Table 1, Entry 36)

TMSOTf (4.5 μL, 0.025 mmol) was added to a solution of **9e** (81.3 mg, 0.12 mmol) and $TMSN_3$ (49.2 μL, 0.37 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **5e** as a white oil. Yield: 74.7 mg (91%).

$[\alpha]_D^{23}$ +58.6 (*c* 3.24, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.17 (d, *J* = 13.9 Hz, 1 H, CCH_aH_bPh), 3.32 (d, *J* = 13.9 Hz, 1 H, CCH_aH_bPh), 3.40 (d, *J* = 9.3 Hz, 1 H, H-3), 3.64 (t, *J* = 9.0 Hz, 1 H, H-5), 3.71 (dd, *J* = 1.7, 11.0 Hz, 1 H, H_a-7), 3.80 (dd, *J* = 3.4, 11.0 Hz, 1 H, H_b-7), 3.85–3.88 (m, 1 H, H-6), 4.01 (t, *J* = 9.2 Hz, 1 H, H-4), 4.52–4.95 (m, 8 H, CH_2Ph), 7.17–7.38 (m, 25 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 41.7 (CCH_2Ph), 68.4 (C-7), 73.2 (CH_2Ph), 73.7 (C-6), 75.0 (CH_2Ph), 75.1 (CH_2Ph), 75.7 (CH_2Ph), 77.7 (C-5), 81.0 (C-3), 83.9 (C-4), 94.3 (C-2), 127.0–138.2 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{41}H_{41}N_3O_5$: 678.2944; found: 678.2951.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-Azido-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-phenyltetrahydropyran (5f) (Table 1, Entry 20)

TMSOTf (7.5 μL, 0.041 mmol) was added to a solution of **1f** (126 mg, 0.20 mmol) and $TMSN_3$ (81.4 μL, 0.61 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed

as for the remaining preparation of **3a**, giving **5f** as a white oil. Yield: 125.6 mg (96%).

$[\alpha]_D^{23}$ +11.1 (*c* 4.02, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.43 (d, *J* = 9.6 Hz, 1 H, H-3), 3.81 (d, *J* = 11.0 Hz, 2 H, H_a-7, C*H*$_2$Ph), 3.89 (t, *J* = 9.6 Hz, 1 H, H-5), 3.91 (dd, *J* = 3.5, 11.0 Hz, 1 H, H_b-7), 4.06 (t, *J* = 9.6 Hz, 1 H, H-4), 4.09–4.10 (m, 1 H, H-6), 4.41–4.92 (m, 7 H, C*H*$_2$Ph), 7.02–7.43 (m, 23 H, Ph), 7.67 (d, 2 H, CPh).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 68.7 (C-7), 73.4 (*C*H$_2$Ph), 74.1 (C-6), 75.1 (*C*H$_2$Ph), 75.7 (*C*H$_2$Ph), 75.8 (*C*H$_2$Ph), 77.9 (C-5), 83.2 (C-4), 84.8 (C-3), 95.7 (C-2), 126.9–138.6 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{40}H_{39}N_3O_5$: 664.2787; found: 664.2750.

(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran-2-carbonitrile (6a) (Table 1, Entry 21)

TMSOTf (4.9 μL, 0.027 mmol) was added to a solution of **1a** (75.9 mg, 0.14 mmol) and TMSCN (54.7 μL, 0.41 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6a**[4b] as a white oil. Yield: 73.4 mg (95%).

(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxy)methyl-2-ethyltetrahydropyran-2-carbonitrile (6b) (Table 1, Entry 22)

TMSOTf (6.8 μL, 0.037 mmol) was added to a solution of **1b** (105.7 mg, 0.19 mmol) and TMSCN (74.4 μL, 0.56 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6b** as a white oil. Yield: 96.1 mg (90%).

$[\alpha]_D^{23}$ +42.2 (*c* 4.72, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.62–1.71 (m, 1 H, $CH_aH_bCH_3$), 2.03–2.12 (m, 1 H, $CH_aH_bCH_3$), 3.35 (d, *J* = 9.3 Hz, 1 H, H-3), 3.68–3.86 (m, 4 H, H-5, H-6, H-7), 3.96 (t, *J* = 9.7 Hz, 1 H, H-4), 4.49–4.96 (m, 8 H, C*H*$_2$Ph), 7.17–7.35 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 7.8 (CH_2CH_3), 29.9 (CH_2CH_3), 68.0 (C-7), 73.3 (*C*H$_2$Ph), 75.0 (*C*H$_2$Ph), 75.4 (*C*H$_2$Ph), 75.8 (*C*H$_2$Ph), 76.5 (C-6), 77.0 (C-5), 79.1 (C-2), 81.0 (C-3), 84.6 (C-4), 117.2 (*C*N), 127.5–138.0 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{37}H_{39}NO_5$: 600.2726; found: 600.2679.

(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxy)methyl-2-butyltetrahydropyran-2-carbonitrile (6c) (Table 1, Entry 23)

TMSOTf (7.8 μL, 0.043 mmol) was added to a solution of **1c** (128.3 mg, 0.21 mmol) and TMSCN (86 μL, 0.64 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6c** as a white oil. Yield: 119.9 mg (92%).

$[\alpha]_D^{23}$ +52.5 (*c* 2.63, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.27 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.48–1.58 (m, 3 H, $CH_aH_bCH_2CH_2CH_3$), 1.90–1.97 (m, 1 H, $CH_aH_bCH_2CH_2CH_3$), 3.34 (d, *J* = 9.3 Hz, 1 H, H-3), 3.67–3.82 (m, 4 H, H-5, H-6, H-7), 3.95 (t, *J* = 9.2 Hz, 1 H, H-4), 4.48–4.96 (m, 8 H, C*H*$_2$Ph), 7.18–7.32 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.4 ($CH_2CH_2CH_2CH_3$), 24.5 ($CH_2CH_2CH_2CH_3$), 25.4 ($CH_2CH_2CH_2CH_3$), 36.2 ($CH_2CH_2CH_2CH_3$), 68.0 (C-7), 73.2 (*C*H$_2$Ph), 75.4 (*C*H$_2$Ph), 75.8 (*C*H$_2$Ph), 75.9 (*C*H$_2$Ph), 76.7 (C-5), 77.0 (C-6), 78.6 (C-2), 81.0 (C-3), 84.6 (C-4), 117.3 (*C*N), 127.5–138.0 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{39}H_{43}NO_5$: 628.3039; found: 628.3005.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-carbonitrile (6d) (Table 1, Entry 24)

TMSOTf (4.5 μL, 0.025 mmol) was added to a solution of **1d** (71.8 mg, 0.12 mmol) and TMSCN (49.5 μL, 0.37 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6d** as a white oil. Yield: 47.4 mg (65%).

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-carbonitrile (6d) (Table 1, Entry 37)

TMSOTf (5.2 μL, 0.029 mmol) was added to a solution of **9d** (89.2 mg, 0.14 mmol) and TMSCN (57.3 μL, 0.43 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6d** as a white oil. Yield: 80.6 mg (95%).

$[\alpha]_D^{23}$ +48.5 (*c* 2.21, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.47–2.51 (m, 1 H, CH_aH_b-$CH{=}CH_2$), 2.72–2.76 (m, 1 H, $CH_aH_bCH{=}CH_2$), 3.41 (d, *J* = 9.0 Hz, 1 H, H-3), 3.69–3.73 (m, 2 H, H-5, H_a-7), 3.80 (dd, *J* = 3.4, 11.0 Hz, 1 H, H_b-7), 3.85–3.86 (m, 1 H, H-6), 3.96 (t, *J* = 10.0 Hz, 1 H, H-4), 4.51–4.97 (m, 8 H, C*H*$_2$Ph), 5.15 (d, *J* = 17.1 Hz, 1 H, $CH_2CH{=}CH_aH_b$), 5.21 (d, *J* = 11.6 Hz, 1 H, $CH_2CH{=}CH_aH_b$), 5.82–5.89 (m, 1 H, $CH_2CH{=}CH_2$), 7.15–7.35 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 40.6 ($CH_2CH{=}CH_2$), 68.0 (C-7), 73.3 (*C*H$_2$Ph), 75.0 (*C*H$_2$Ph), 75.2 (*C*H$_2$Ph), 75.8 (*C*H$_2$Ph), 76.7 (C-6), 76.8 (C-5), 78.3 (C-2), 80.3 (C-3), 84.7 (C-4), 117.1 (*C*N), 120.5 ($CH_2CH{=}CH_2$), 127.5–128.4 (Ph), 130.3 ($CH_2CH{=}CH_2$), 137.5–138.1 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{38}H_{39}NO_5$: 612.2726; found: 612.2690.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-carbonitrile (6e) (Table 1, Entry 25)

TMSOTf (5.7 μL, 0.031 mmol) was added to a solution of **1e** (99.5 mg, 0.16 mmol) and TMSCN (63.1 μL, 0.47 mmol) in MeCN (2 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6e** as a white oil. Yield: 74.1 mg (73%).

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-carbonitrile (6e) (Table 1, Entry 38)

TMSOTf (4.1 μL, 0.023 mmol) was added to a solution of **9e** (75.9 mg, 0.11 mmol) and TMSCN (45.1 μL, 0.34 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **6e** as a white oil. Yield: 61.8 mg (86%).

$[\alpha]_D^{23}$ +34.7 (*c* 1.2, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.95 (d, *J* = 14.2 Hz, 1 H, CCH_aH_b-Ph), 3.25 (d, *J* = 14.1 Hz, 1 H, CCH_aH_bPh), 3.39 (d, *J* = 9.6 Hz, 1 H, H-3), 3.65–3.78 (m, 4 H, H-5, H-6, H-7), 3.99 (t, *J* = 9.1 Hz, 1 H, H-4), 4.53–5.03 (m, 8 H, C*H*$_2$Ph), 7.22–7.37 (m, 25 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 42.2 (C*C*H$_2$Ph), 68.0 (C-7), 73.3 (*C*H$_2$Ph), 75.0 (*C*H$_2$Ph), 75.2 (*C*H$_2$Ph), 75.9 (*C*H$_2$Ph), 76.5 (C-6), 77.0 (C-5), 79.0 (C-2), 80.3 (C-3), 84.8 (C-4), 116.8 (*C*N), 127.4–138.0 (Ph).

HRMS (ESI): *m*/*z* [M + Na$^+$] calcd for $C_{42}H_{41}NO_5$: 662.2882; found: 662.2913.

1-Phenyl-2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-methyltetrahydropyran-2-yl]ethanone (7a) (Table 1, Entry 26)

TMSOTf (6.8 μL, 0.037 mmol) was added to a solution of **1a** (119 mg, 0.21 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (132 μL, 0.64 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7a**[4b] as a white oil. Yield: 137.4 mg (98%).

1-Phenyl-2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-ethyltetrahydropyran-2-yl]ethanone (7b) (Table 1, Entry 27)

TMSOTf (6.8 μL, 0.037 mmol) was added to a solution of **1b** (105.9 mg, 0.19 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (114.5 μL, 0.56 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7b** as a white oil. Yield: 112.0 mg (91%).

$[\alpha]_D^{23}$ +35.7 (*c* 3.47, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.3 Hz, 3 H, CH$_2$C*H*$_3$), 1.76–1.80 (m, 1 H, C*H*$_a$H$_b$CH$_3$), 1.84–1.88 (m, 1 H, CH$_a$*H*$_b$CH$_3$), 3.09 (d, *J* = 14.4 Hz, 1 H, C*H*$_a$H$_b$COPh), 3.61 (d, *J* = 14.4 Hz, 1 H, CH$_a$*H*$_b$COPh), 3.64 (d, *J* = 9.3 Hz, 1 H, H-3), 3.66–3.69 (m, 1 H, H$_a$-7), 3.72 (t, *J* = 9.3 Hz, 1 H, H-5), 3.82 (dd, *J* = 3.6, 11.3 Hz, 1 H, H$_b$-7), 3.88–3.92 (m, 1 H, H-6), 3.92 (t, *J* = 9.1 Hz, 1 H, H-4), 4.50–4.90 (m, 8 H, C*H*$_2$Ph), 7.19–7.96 (m, 25 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.5 (CH$_2$*C*H$_3$), 29.7 (*C*H$_2$CH$_3$), 36.9 (*C*H$_2$COPh), 69.0 (C-7), 72.9 (C-6), 73.3 (*C*H$_2$Ph), 75.0 (*C*H$_2$Ph), 75.2 (*C*H$_2$Ph), 75.4 (*C*H$_2$Ph), 78.8 (C-5), 79.8 (C-2), 80.7 (C-3), 84.0 (C-4), 127.3–138.8 (Ph), 198.4 (CH$_2$*C*OPh).

HRMS (ESI): *m*/*z* [M + Na$^+$] calcd for $C_{44}H_{46}O_6$: 693.3192; found: 693.3144.

1-Phenyl-2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-butyltetrahydropyran-2-yl]ethanone (7c) (Table 1, Entry 28)

TMSOTf (7.4 μL, 0.041 mmol) was added to a solution of **1c** (121 mg, 0.20 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (124.7 μL, 0.61 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7c** as a white oil. Yield: 123.6 mg (87%).

$[\alpha]_D^{23}$ +23.3 (*c* 3.47, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 6.9 Hz, 3 H, CH$_2$CH$_2$CH$_2$C*H*$_3$), 1.18–1.28 (m, 3 H, CH$_2$C*H*$_a$H$_b$C*H*$_2$CH$_3$), 1.43–1.53 (m, 1 H, CH$_2$CH$_a$*H*$_b$CH$_2$CH$_3$), 1.68–1.84 (m, 2 H, C*H*$_2$CH$_2$CH$_2$CH$_3$), 3.10 (d, *J* = 14.4 Hz, 1 H, C*H*$_a$H$_b$COPh), 3.59 (d, *J* = 14.4 Hz, 1 H, CH$_a$*H*$_b$COPh), 3.64 (d, *J* = 9.3 Hz, 1 H, H-3), 3.65 (d, *J* = 11.0 Hz, 1 H, H$_a$-7), 3.70 (t, *J* = 9.6 Hz, 1 H, H-5), 3.80 (dd, *J* = 3.6, 11.1 Hz, 1 H, H$_b$-7), 3.84–3.89 (m, 1 H, H-6), 3.91 (t, *J* = 9.3 Hz, 1 H, H-4), 4.51–4.90 (m, 8 H, C*H*$_2$Ph), 7.19–7.88 (m, 25 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH$_2$CH$_2$CH$_2$*C*H$_3$), 23.0 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 25.2 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 36.9 (*C*H$_2$COPh), 37.1 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 69.0 (C-7), 72.9 (C-6), 73.3 (*C*H$_2$Ph), 75.0 (*C*H$_2$Ph), 75.2 (*C*H$_2$Ph), 75.3 (*C*H$_2$Ph), 78.8 (C-5), 79.8 (C-2), 81.3 (C-3), 84.0 (C-4), 127.2–138.9 (Ph), 198.3 (CH$_2$*C*OPh).

HRMS (ESI): *m*/*z* [M + Na$^+$] calcd for $C_{46}H_{50}O_6$: 721.3505; found: 721.3552.

2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-yl]-1-phenylethanone (7d) (Table 1, Entry 29)

TMSOTf (7.3 μL, 0.04 mmol) was added to a solution of **1d** (117.1 mg, 0.2 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (124 μL, 0.6 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7d** as a white oil. Yield: 72.7 mg (53%).

2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-yl]-1-phenylethanone (7d) (Table 1, Entry 39)

TMSOTf (5.8 μL, 0.032 mmol) was added to a solution of **9d** (99.2 mg, 0.16 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (98 μL, 0.47 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7d** as a white oil. Yield: 100.5 mg (93%).

$[\alpha]_D^{23}$ +43.1 (*c* 3.48, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (dd, *J* = 9.3, 14.4 Hz, 1 H, C*H*$_a$H$_b$CH=CH$_2$), 2.52 (dd, *J* = 9.3, 14.6 Hz, 1 H, CH$_a$*H*$_b$CH=CH$_2$), 3.02 (d, *J* = 14.6 Hz, 1 H, C*H*$_a$H$_b$COPh), 3.40 (d, *J* = 14.4 Hz, 1 H, CH$_a$*H*$_b$COPh), 3.46–3.49 (m, 1 H, H$_a$-7), 3.50 (d, *J* = 9.0 Hz, 1 H, H-3), 3.53 (t, *J* = 9.3 Hz, 1 H, H-5), 3.62 (dd, *J* = 3.4, 11.3 Hz, 1 H, H$_b$-7), 3.70–3.73 (m, 1 H, H-6), 3.73 (t, *J* = 9.0 Hz, 1 H, H-4), 4.33–4.73 (m, 8 H, C*H*$_2$Ph), 4.84–4.92 (m, 2 H, CH$_2$CH=C*H*$_2$), 5.74–5.85 (m, 1 H, CH$_2$C*H*=CH$_2$), 7.01–7.77 (m, 25 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.9 (*C*H$_2$COPh), 41.6 (*C*H$_2$CH=CH$_2$), 68.9 (C-7), 73.0 (C-6), 73.3 (*C*H$_2$Ph), 74.8 (*C*H$_2$Ph), 74.9 (*C*H$_2$Ph), 75.3 (*C*H$_2$Ph), 78.7 (C-5), 79.9 (C-2), 81.3 (C-3), 83.8 (C-4), 118.4 (CH$_2$CH=*C*H$_2$), 127.2–132.9 (Ph), 133.8 (CH$_2$*C*H=CH$_2$), 136.9–138.7 (Ph), 198.2 (CH$_2$*C*OPh).

Anal. Calcd for $C_{45}H_{46}O_6$: C, 79.15; H, 6.79. Found: C, 78.79; H, 6.74.

2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-yl]-1-phenylethanone (7e) (Table 1, Entry 30)

TMSOTf (6.8 μL, 0.037 mmol) was added to a solution of **1e** (117.9 mg, 0.19 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (115 μL, 0.56 mmol) in MeCN (3.0 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7e** as a white oil. Yield: 83.7 mg (61%).

2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran-2-yl]-1-phenylethanone (7e) (Table 1, Entry 40)

TMSOTf (2.7 μL, 0.015 mmol) was added to a solution of **9e** (50.4 mg, 0.075 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (46.1 μL, 0.22 mmol) in MeCN–CH_2Cl_2 (1:1, 2 mL) at –78 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 2 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7e** as a white oil. Yield: 46.4 mg (91%).

$[\alpha]_D^{23}$ +34.2 (*c* 2.85, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.05 (d, *J* = 14.4 Hz, 1 H, CC*H*$_a$H$_b$-Ph), 3.22 (d, *J* = 14.4 Hz, 1 H, C*H*$_a$H$_b$COPh), 3.30 (d, *J* = 14.1 Hz, 1 H, CCH$_a$*H*$_b$Ph), 3.47 (d, *J* = 9.0 Hz, 1 H, H-3), 3.63 (d, *J* = 9.3 Hz, 1 H, H-5), 3.69 (d, *J* = 14.4 Hz, 1 H, CH$_a$*H*$_b$COPh), 3.71–3.73 (m,

1 H, H_a-7), 3.82 (dd, *J* = 3.1, 10.8 Hz, 1 H, H_b-7), 3.89–3.93 (m, 2 H, H-4, H-6), 4.51–4.86 (m, 8 H, CH_2Ph), 7.09–7.96 (m, 30 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.6 (*C*H_2COPh), 43.1 (C*C*H_2Ph), 69.2 (C-7), 72.8 (C-6), 73.2 (*C*H_2Ph), 74.4 (*C*H_2Ph), 74.8 (*C*H_2Ph), 75.2 (*C*H_2Ph), 78.6 (C-5), 80.4 (C-3), 80.7 (C-2), 84.0 (C-4), 126.3–138.8 (Ph), 198.5 (CH_2*C*OPh).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{49}H_{48}O_6$: 755.3349; found: 755.3376.

1-Phenyl-2-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyl-2-phenyltetrahydropyran-2-yl]ethanone (7f) (Table 1, Entry 31)

TMSOTf (6.9 μL, 0.038 mmol) was added to a solution of **1f** (116.8 mg, 0.19 mmol) and 1-phenyl-1-(trimethylsiloxy)ethene (109.3 μL, 0.53 mmol) in MeCN (3 mL) at –40 °C in the presence of $CaSO_4$ (ca. 100 mg). The resulting mixture was stirred for 3 h, and then the same procedure was followed as for the remaining preparation of **3a**, giving **7f** as a white oil. Yield: 105.5 mg (78%).

$[\alpha]_D^{23}$ +33.9 (*c* 4.39, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.47 (d, *J* = 8.9 Hz, 1 H, H-3), 3.71 (d, *J* = 17.2 Hz, 1 H, C$H_a$$H_b$COPh), 3.77 (dd, *J* = 1.4, 11.0 Hz, 1 H, H_a-7), 3.85–3.87 (m, 1 H, H-6), 3.89 (dd, *J* = 2.8, 10.3 Hz, 1 H, H_b-7), 3.91 (d, *J* = 10.3 Hz, 1 H, CH_2Ph), 3.92 (d, *J* = 9.6 Hz, 1 H, H-5), 4.00 (t, *J* = 9.6 Hz, 1 H, H-4), 4.14 (d, *J* = 17.2 Hz, 1 H, $CH_a$$H_b$COPh), 4.59–4.95 (m, 7 H, CH_2Ph), 7.17–7.44 (m, 26 H, Ph), 7.61 (d, *J* = 6.9 Hz, 2 H, CPh), 7.77 (d, *J* = 6.9 Hz, 2 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.0 (*C*H_2COPh), 69.1 (C-7), 73.1 (C-6), 73.5 (*C*H_2Ph), 75.1 (*C*H_2Ph), 75.5 (*C*H_2Ph), 75.7 (*C*H_2Ph), 78.6 (C-5), 79.5 (C-2), 84.2 (C-4), 86.8 (C-3), 125.7–143.4 (Ph), 196.3 (CH_2*C*OPh).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{48}H_{46}O_6$: 741.3192; found: 741.3188.

(2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxy)methyl-2-butyltetrahydropyran-2-ol (1c)

To a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (1.0037 g, 1.86 mmol) in THF (10 mL) at –78 °C was added 1.5 M *n*-BuLi in *n*-hexane (1.46 mL, 2.23 mmol) under an Ar atmosphere, and the mixture was stirred for 2 h. The reaction was then quenched with H_2O (15 mL). The mixture was extracted with $CHCl_3$, and the organic layer was washed with H_2O and sat. NaCl soln. After the organic layer was dried (Na_2SO_4), the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, EtOAc–hexane, 1:8) to give **1c** as a white oil. Yield: 1.0562 g (95%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.24–1.25 (m, 3 H, $CH_2CH_aH_bCH_2CH_3$), 1.33–1.40 (m, 1 H, $CH_2CH_aH_bCH_2CH_3$), 1.63–1.66 (m, 2 H, $CH_2CH_2CH_2CH_3$), 2.68 (s, 1 H, OH), 3.43 (d, *J* = 8.9 Hz, 1 H, H-3), 3.64 (t, *J* = 9.6 Hz, 1 H, H-5), 3.66 (dd, *J* = 3.4, 9.6 Hz, 1 H, H_a-7), 3.74 (dd, *J* = 4.1, 11.0 Hz, 1 H, H_b-7), 3.99 (dd, *J* = 2.0, 12.2 Hz, 1 H, H-6), 4.01 (t, *J* = 8.9 Hz, 1 H, H-4), 4.52–4.93 (m, 8 H, CH_2Ph), 7.19–7.34 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.0 ($CH_2CH_2CH_2CH_3$), 22.8 ($CH_2CH_2CH_2CH_3$), 24.7 ($CH_2CH_2CH_2CH_3$), 38.3 ($CH_2CH_2CH_2CH_3$), 68.8 (C-7), 71.5 (C-6), 73.2 (*C*H_2Ph), 74.8 (*C*H_2Ph), 75.3 (*C*H_2Ph), 75.5 (*C*H_2Ph), 78.5 (C-5), 81.3 (C-3), 83.8 (C-4), 98.4 (C-2), 126.9–138.6 (Ph).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{38}H_{44}O_6$: 619.3030; found: 619.3036.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Acetoxy-2-allyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (9d)

To a solution of **1d** (417.3 mg, 0.72 mmol) in dry THF (5 mL) at –78 °C was added 1.6 M *n*-BuLi in *n*-hexane (0.54 mL, 0.86 mmol) under an Ar atmosphere, and the mixture was stirred for 1 h. The temperature was gradually raised to –20 °C, and Ac_2O (1.2 mL, 12.7 mmol) was added to the solution. The resulting mixture was stirred for 1 h. The reaction was then quenched with sat. $NaHCO_3$ soln (15 mL). The mixture was extracted with EtOAc, and the organic layer was washed with H_2O and sat. NaCl soln. After the organic layer was dried (Na_2SO_4), the solvent was evaporated under reduced pressure. The crude product was purified by preparative TLC (silica gel, EtOAc–hexane, 1:4) to give **9d** as a white oil. Yield: 367.7 mg (82%).

$[\alpha]_D^{23}$ +78.2 (*c* 2.61, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.89 (dd, *J* = 9.0, 15.0 Hz, 1 H, C$H_a$$H_b$CH=$CH_2$), 3.42 (dd, *J* = 5.0, 15.0 Hz, 1 H, $CH_a$$H_b$CH=$CH_2$), 3.52 (d, *J* = 9.0 Hz, 1 H, H-3), 3.64 (d, *J* = 9.0 Hz, 1 H, H-6), 3.71 (d, *J* = 11.0 Hz, 1 H, H_a-7), 3.80 (t, *J* = 9.0 Hz, 1 H, H-5), 3.83 (dd, *J* = 2.8, 11.0 Hz, 1 H, H_b-7), 4.01 (t, *J* = 9.0 Hz, 1 H, H-4), 4.53–4.92 (m, 8 H, CH_2Ph), 5.07–5.10 (m, 2 H, CH_2CH=CH_2), 5.86–5.88 (m, 1 H, CH_2C*H*=CH_2), 7.17–7.36 (m, 20 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.2 (*C*H_3), 38.4 (*C*H_2CH=CH_2), 68.2 (C-7), 73.4 (*C*H_2Ph), 73.5 (C-6), 75.1 (2 *C*H_2Ph), 75.4 (*C*H_2Ph), 77.6 (C-5), 80.8 (C-3), 83.0 (C-4), 105.7 (C-2), 118.7 (CH_2CH=*C*H_2), 127.5–128.4 (Ph), 132.6 (CH_2*C*H=CH_2), 137.9–138.4 (Ph), 168.6 (*C*=O).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{39}H_{42}O_7$: 645.2828; found: 645.2811.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Acetoxy-2-benzyl-3,4,5-tris(benzyloxy)-6-(benzyloxy)methyltetrahydropyran (9e)

To a solution of **1e** (362.2 mg, 0.57 mmol) in THF (6 mL) at –78 °C was added 1.6 M *n*-BuLi in *n*-hexane (0.43 mL, 0.68 mmol) under an Ar atmosphere, and the mixture was stirred for 1 h. The temperature was gradually raised to –20 °C, and Ac_2O (0.6 mL, 6.3 mmol) was added to the solution. The resulting mixture was stirred for 1 h, and then the same procedure was followed as for the remaining preparation of **9d**, giving **9e** as a white oil. Yield: 364.1 mg (94%).

$[\alpha]_D^{23}$ +46.1 (*c* 1.40, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, CH_3), 3.25 (d, *J* = 13.7 Hz, 1 H, CC$H_a$$H_b$Ph), 3.30 (d, *J* = 8.9 Hz, 1 H, H-3), 3.67–3.70 (m, 1 H, H-6), 3.73 (t, *J* = 9.0 Hz, 1 H, H-5), 3.80 (dd, *J* = 2.0, 11.0 Hz, 1 H, H_a-7), 3.87 (dd, *J* = 2.8, 11.0 Hz, 1 H, H_b-7), 4.03 (t, *J* = 8.9 Hz, 1 H, H-4), 4.20 (d, *J* = 13.8 Hz, 1 H, $CCH_a$$H_b$Ph), 4.40–4.90 (m, 8 H, CH_2Ph), 7.15–7.37 (m, 25 H, Ph).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.4 (*C*H_3), 39.9 (C*C*H_2Ph), 68.5 (C-7), 73.3 (*C*H_2Ph), 73.6 (C-6), 74.5 (*C*H_2Ph), 75.2 (*C*H_2Ph), 75.4 (*C*H_2Ph), 77.6 (C-5), 79.5 (C-3), 83.3 (C-4), 106.8 (C-2), 126.6–138.8 (Ph), 168.9 (*C*=O).

HRMS (ESI): *m*/*z* [M + Na^+] calcd for $C_{43}H_{44}O_7$: 695.2985; found: 695.2944.

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