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# A neighboring group participation strategy: direct and highly diastereoselective synthesis of 2-substituted and 2,2-bisubstituted perhydrofuro-[2,3-*b*]pyran derivatives†

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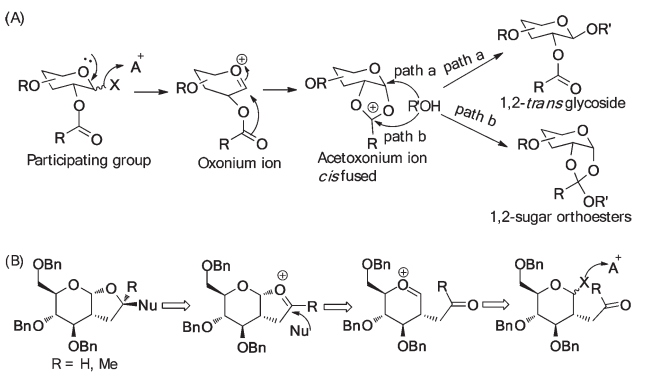
Treatment of methyl 2-*C*-formylmethyl-2-deoxy-β-D-glucopyranoside (**5**) or methyl 2-*C*-acetylmethyl-2-deoxy-β-D-glucopyranoside (**1**) with $H_2SO_4$–HOAc–$Ac_2O$ gave 2-acetoxyl-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]hexahydrofuro[2,3-*b*]pyran (**6**) and acetyl 2-*C*-acetylmethyl-2-deoxy-α-D-glucopyranoside (**7**) respectively, which were further reacted with nucleophiles in the presence of TMSOTf and offered a series of 2-substituted and 2,2-disubstituted perhydrofuro[2,3-*b*]pyran derivatives in high yield with excellent diastereoselectivity.

## Introduction

The perhydrofuro[2,3-*b*]pyran scaffolds constitute the core structural elements which are prevalent in a large number of naturally occurring biological active products.[1] Recent research also revealed that they would be used as potential HIV-1 protease inhibitors.[2] Among the myriad of elegant approaches to construct perhydrofuro[2,3-*b*]pyrans,[3] intramolecular cyclizations are particularly attractive with regard to stereoselectivity and chemoselectivity.[4] To this end, several different intramolecular cyclization strategies have been introduced to achieve the synthesis of substituted perhydrofuro[2,3-*b*]pyrans. Particularly, the use of 3-halogeno-2-allyloxy-perhydropyrans as substrates *via* radical cyclization to synthesize 3-substituted perhydrofuro[2,3-*b*]pyrans have been extensively studied and used to construct a number of complex natural or unnatural products.[5] Furthermore, in 2003, Yus and co-workers successfully synthesized 2,2-dialkyl-substituted perhydrofuro[2,3-*b*]-pyrans *via* the oxidation–cyclization of methylidenic diols.[6] Very recently, Chandrasekaran and co-workers achieved the synthesis of 3-idio-perhydrofuro[2,3-*b*]pyrano-γ-butyrolactones and 3-idio-perhydrofuro[2,3-*b*]pyrans *via* NIS-mediated ring opening of 1,2-cyclopropanated sugar derivatives.[7] In most of these cases, much attention has been paid to the synthesis of 3-substituted perhydrofuro[2,3-*b*]pyrans. Installation of a heteroatom substituent or an active functional group at the C(2) position of perhydrofuro[2,3-*b*]pyran, however, still represents a great challenge.

On the other hand, the use of neighboring group participation for regio- and stereo-chemical control is ubiquitous in organic chemistry.[8] Nowhere is this strategy more extensively exploited than in carbohydrate chemistry.[9] Neighboring group participation of a 2-*O*-carboxylate ester is the most reliable method for stereoselective construction of the 1,2-*trans* glycosidic bond. Generally, in this strategy, a 2-*O*-carboxylate ester and an anomeric leaving group must be installed first (Scheme 1(A)). Then, in the presence of a promoter, the




**Scheme 1** (A) The neighboring group participation strategy in the synthesis of 1,2-*trans*-glycosides. (B) The construction of perhydrofuro[2,3-*b*]-pyrans *via* a neighboring group participation strategy.

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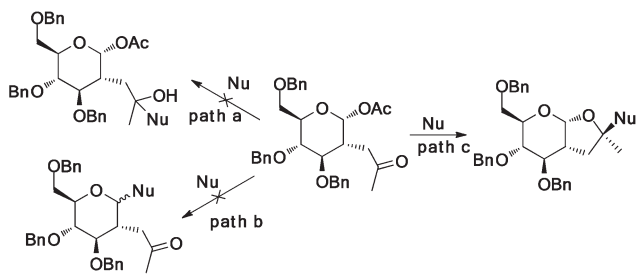
leaving group is activated, followed by its departure with the help of the oxygen of the pyran-ring to form an oxonium ion. Then, the carbonyl group attacked the oxonium ion forming a more stable acetoxonium ion. An alcohol can attack the anomeric center of the acetoxonium ion from only one face to provide 1,2-*trans* glycoside (Scheme 1(A), path a). An unavoidable by-product associated with this reaction is 1,2-sugar orthoester derived from the attack of the alcohol to the acetoxonium ion (Scheme 1(A), path b).

Furthermore, it is well established that the 2-*C*-branched (acetylmethyl or acetonyl) sugars are the C2-carbon isosteres of the 2-*O*-acetyl-sugars or 2-*N*-acetamido sugars,[10] and the 2-*C*-branched sugars have been widely used in glycobiology.[10d–f] Inspired by the neighboring group participation phenomenon and due to our continued interest in the construction of 2-*C*-branched glycoside,[11] it was assumed that the perhydrofuro[2,3-*b*]pyran derivatives would be obtained from the nucleophilic capture of the bicyclic oxocarbenium ion, which could be generated through the attack of the 2-carbonyl oxygen of the 2-formylmethyl or 2-acetylmethyl to the anomeric center (Scheme 1(B)). By this strategy, recently, we have reported a highly stereoselective synthesis of 2-*O*/*N* substituted perhydrofuro[2,3-*b*]pyran derivatives from *p*-tolyl 2-formylmethyl-2-deoxy-D-thioglucopyranoside.[11c] Mechanistic studies demonstrated that the formation of 2-*O*/*N* substituted perhydrofuro[2,3-*b*]pyran derivatives was partially through a $S_N2$-type reaction. Furthermore, we also successfully constructed the 2,2-disubstituted perhydrofuro[2,3-*b*]pyran (and furan) derivatives starting from 1,2-cyclopropanated sugars *via* ring-opening-recyclization–addition in the presence of $BiCl_3$.[12] As a continuation of these studies, herein, we describe the synthesis of 2-*C*-substituted and 2,2-disubstituted perhydrofuro-[2,3-*b*]pyran derivatives using 2-formylmethyl/2-acetylmethyl instead of 2-*O*-acetyl as a participating group, and the formation of 2,2-disubstituted perhydrofuro[2,3-*b*]pyran derivatives was a $S_N1$-type reaction.

The potential advantage of this approach over the previous methods was that the products could be further converted to other fused-ring derivatives conveniently due to the presence of allyl, carbonyl and cyano groups. Also, both the chemoselectivity and stereoselectivity are excellent, and there may be three different reaction pathways for nucleophiles keto carbonyl (Scheme 2, path a) *vs.* anomeric oxocarbenium ion (Scheme 2, path b) *vs.* a 6/5 fused bicyclic oxocarbenium ion (Scheme 2, path c), however, we only obtained the fused-cyclic products in high yield with only one diastereoisomer (when TMSCN was used as a nucleophile, two diastereoisomers were obtained). Furthermore, it is well established that the neighboring group participation is not a predominant factor in the synthesis of *C*-glycosides,[13] interestingly, our research demonstrated that it is possible to use neighboring group participation to highly selectively construct a fused-ring by slightly changing the structure of the substrate. Besides, these carbohydrate-based fused-cyclic compounds could be used to mimic the transition state geometry of glycosidases or glycosyltransferases,[14] thus they can be further tested as potential small-molecule inhibitors of glycosidases or glycosyltransferases.[15] Finally, this method furnished the products containing a chiral quaternary carbon center in a stereoselective manner, which is perceived as a challenging problem in organic synthesis.[16] These features make it an exceedingly efficient and practical method for synthesis of 2-substituted and 2,2-disubstituted perhydrofuro-[2,3-*b*]pyran derivatives.

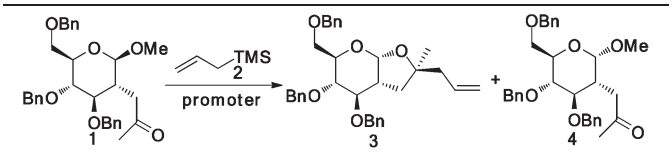



Scheme 2 The different reaction pathways between acetyl 2-*C*-acetylmethyl-α-D-glucopyranoside and nucleophiles.

## Results and discussion

Initially, we selected the methyl 2-*C*-acetylmethyl-2-deoxy-β-D-glucopyranoside **1**[11h] and allyltrimethylsilane **2** as the model substrates to screen reaction conditions, the results are summarized in Table 1. As shown in Table 1, when 2.0 equiv. of TMSOTf and $BF_3{\cdot}OEt_2$ were used at −78 °C to r.t., we obtained the bicyclic compound **3** in 75% and 62% yield respectively (Table 1, entries 1 and 2). In contrast, some other Lewis acids including $ZnCl_2$, $AlCl_3$, and $FeCl_3$ only gave disappointing

Table 1 Optimal of the reaction conditions[a]



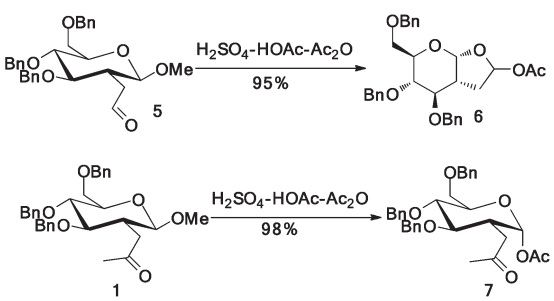

| Entry | Promoter | Solvent | *T* | Product[b] |
|---|---|---|---|---|
| 1[c] | TMSOTf | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | **3** (75%) |
| 2[c] | $BF_3{\cdot}OEt_2$ | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | **3** (62%) |
| 3[c] | $ZnCl_2$ | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | NR |
| 4[c] | $AlCl_3$ | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | Trace |
| 5[c] | $FeCl_3$ | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | Decomposed |
| 6[c] | $BiCl_3$ | $CH_2Cl_2$ | −78 °C to r.t. (15 h) | **3** (54%) |
| **7**[d] | **TMSOTf** | **$CH_3CN$** | **−40 °C to r.t. (2 h)** | **3 (84%)** |
| 8 | TMSOTf | $CH_2Cl_2$ | −40 °C to r.t. (18 h) | **4** |
| 9 | TMSOTf | $CHCl_3$ | −40 °C to r.t. (18 h) | **4** |
| 10[d] | TMSOTf | $Et_2O$ | −40 °C to r.t. (18 h) | **4** |
| 11[d] | TMSOTf | Toluene | −40 °C to r.t. (18 h) | **4** |
| 12[d] | TMSOTf | THF | −40 °C to r.t. (18 h) | **4** |
| 13[d] | TMSOTf | DMF | −40 °C to r.t. (18 h) | **4** |
| 14[d] | TMSOTf | Acetone | −40 °C to r.t. (18 h) | **4** |

[a] All reactions were performed with methyl-glucoside **1** (0.1 mmol), allyltrimethylsilane **2** (0.2 mmol), 4 Å M.S. 100 mg. [b] Isolated yield. [c] 2.0 equiv. of promoter were used. [d] 0.8 equiv. of promoter was used.

results (Table 1, entries 3–5). Interestingly, when we conducted the reaction in the presence of 2.0 equiv. of $BiCl_3$ in $CH_2Cl_2$ at −78 °C to r.t., we also obtained the 2,2-disubstituted perhydrofuro[2,3-*b*]pyran derivative in 54% yield (Table 1, entry 6).[12] Further optimization of the reaction conditions showed that the solvent has a great influence on this reaction. For example, we obtained the fused bicyclic product in 84% yield when the reaction was carried out in $CH_3CN$ in the presence of 0.8 equiv. of TMSOTf (Table 1, entry 7); however, other solvents such as $CH_2Cl_2$,[17] $CHCl_3$, $Et_2O$, toluene, THF, DMF and acetone only isomerized methyl 2-*C*-acetylmethyl-2-deoxy-β-D-glucopyranoside (**1**) to the methyl 2-*C*-acetylmethyl-2-deoxy-α-D-glucopyranoside (**4**) (Table 1, entries 8–14). In all cases, we could not avoid the presence of α-D-glucopyranoside **4** even when the reaction was carried out at −40 °C to r.t. for two days.

The methoxy group is not a good leaving group, which may lead to its isomerization.[18] Therefore, we further optimized the substrate by changing the methoxy group to the acetoxyl group. Interestingly, when methyl 2-*C*-formylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyranoside (**5**) was treated with $H_2SO_4$–HOAc–$Ac_2O$,[19] we only obtained the fused-ring product **6**, while under the same reaction conditions methyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyranoside (**1**) was transformed to acetyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyranoside (**7**) smoothly (Scheme 3).

As desired, started from **6**, the fused-ring products were obtained in high yield as a single diastereoisomer except when TMSCN was used as a nucleophile. Inspired by the initial success, under the optimal reaction conditions, acetyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyranoside (**7**) was further treated with 0.8 equiv. of TMSOTf in the presence of nucleophiles. The nucleophiles included allyltrimethylsilane (**2**) and its analogue **9**, silyl enol ether derivates (**15**, **17**, **19**, and **21**) and TMSCN (**11**), the results are summarized in Table 2. Satisfactorily, the coupling reaction between **7** and the nucleophiles could proceed smoothly to furnish the 2,2-disubstituted perhydrofuro[2,3-*b*]pyrans in excellent yield with high stereoselectivity. However, when TMSCN was employed as a nucleophile, two isomers were obtained. The low selectivity of nucleophilic attack exhibited by trimethylsilyl cyanide can be explained by the high reactivity of the nucleophile, and smaller steric hindrance presented by this nucleophile may bring about the lower stereoselectivity as well.[20]




**Scheme 3** Synthesis of acetate from methyl 2-*C*-branched-glycoside.

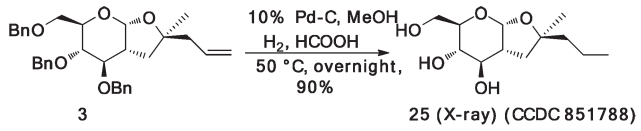
**Table 2** The synthesis of 2-substituted and 2,2-disubstituted perhydrofuro[2,3-*b*]pyrans[a]

| Entry | Donor | Nu | Product | Yield[b] (%) |
|---|---|---|---|---|
| 1 | **6** | TMS, **2** | BnO, BnO, OBn, O, O, **8** | 75 |
| 2 | **6** | TMS, **9** | BnO, BnO, OBn, O, O, **10** | 85 |
| 3 | **6** | TMSCN (**11**) | BnO, BnO, OBn, O, O, CN, **12** | 62 |
| | | | BnO, BnO, OBn, O, O, CN, **13** | 24 |
| 4 | **7** | TMS, **2** | BnO, BnO, OBn, O, O, **3** | 89 |
| 5 | **7** | TMS, **9** | BnO, BnO, OBn, O, O, **14** | 81 |
| 6 | **7** | OTMS, **15** | BnO, BnO, OBn, O, O, **16** | 92 |
| 7 | **7** | OTMS, **17** | BnO, BnO, OBn, O, O, **18** | 95[c] |
| 8 | **7** | OTMS, **19** | BnO, BnO, OBn, O, O, **20** | 86 |
| 9 | **7** | OTMS, **21** | BnO, BnO, OBn, O, O, **22** | 95 |
| 10 | **7** | TMSCN (**11**) | BnO, BnO, OBn, O, O, CN, **23** | 58 |
| | | | BnO, BnO, OBn, O, O, CN, **24** | 32 |

[a] All reactions were carried out using 2.0 equiv. nucleophile, 0.8 equiv. TMSOTf in $CH_3CN$ at −40 °C to r.t. with 100 mg of 4 Å M.S. unless otherwise noted. [b] Isolated yield. [c] A pair of inseparable diastereoisomers (1 : 1) were obtained due to the prochiral centre of the substituted cyclohexanone as determined by $^1H$ NMR.

The stereochemistry of the products was first confirmed by the extensive NMR experiments ($^1$H-NMR, $^{13}$C-NMR, and NOESY) of compounds **3**, **8**, **12**, **18**, **23** and **24** and further determined by X-ray crystallographic analysis of compound **25** (hydrogenation loss of the benzyl product of **3**) (Scheme 4) (Fig. 1).[21]

Based on the results of the experiments, a plausible mechanism is proposed for the formation of perhydrofuro[2,3-*b*]-pyrans (Scheme 5). Starting from acetyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyranoside **7**, TMSOTf coordinated to the carbonyl oxygen atom of OAc and enhanced its leaving ability, followed by its departure with the assistance of oxygen from the pyranoid ring formed the 2-*C*-branched monocyclic pyran oxocarbenium ion. Subsequently, the carbonyl oxygen of the ketone served as an intramolecular nucleophile which attacked the anomeric carbon from α (path-2) or β (path-1) face to form six–five fused-ring oxocarbenium ion intermediates **INT1** or **INT2** respectively.[22] The DFT calculations[23] on the B3LYP/6-31+G** level showed that **INT1** is 8.7 kcal mol$^{-1}$ more stable than **INT2**. Therefore, the major ring oxocarbenium ion is **INT1**. For the 2-acetoxyl-perhydrofuro[2,3-*b*]pyran **6**, in the presence of TMSOTf, it can form the **INT1** directly. Thus, after the formation of **INT1**, theoretically, the nucleophiles can approach the **INT1** from either the concave or convex face to produce the *endo*- or *exo*-products respectively. However, the calculation demonstrated the concave face is more sterically hindered than the convex face,[22] thus the major products of this reaction are *exo*-products, which are consistent with the experimental observations.




**Scheme 4** The hydrogenation loss of benzyl of products **3**.

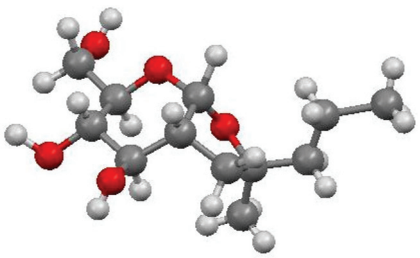
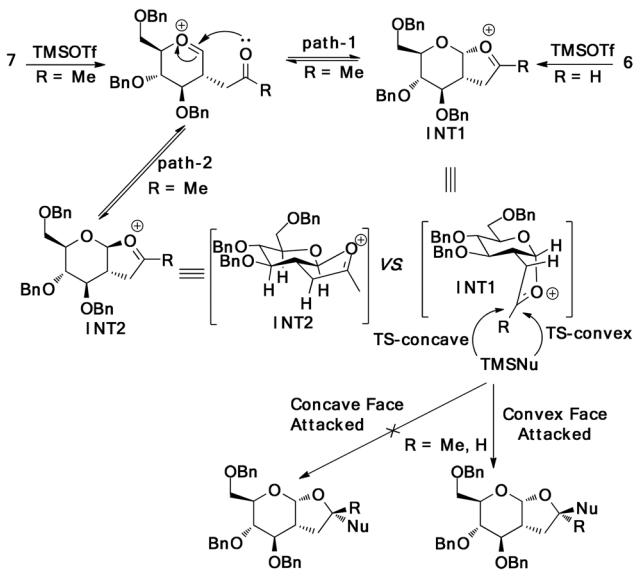


**Fig. 1** X-ray crystal structure of **25**.




**Scheme 5** Plausible mechanism for the synthesis of perhydrofuro[2,3-*b*]pyrans from 2-*C*-branched sugar.

It is worth mentioning that in our previous report, we observed that the *p*-tolyl 2-*C*-formylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside can be used to synthesize 2-*O*/*N* substituted perhydrofuro[2,3-*b*]pyran partially through a $S_N2$-type reaction.[11c] However, in this study, when acetyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside was employed as the starting material, the 2,2-di-substituted perhydrofuro[2,3-*b*]-pyran can still be obtained in high yield with excellent diastereoselectivity, and this is a $S_N1$-type reaction, which means that the reaction proceeds in the different mechanisms by using various substrates.

## Conclusions

In summary, a highly stereoselective synthesis of 2-substituted and 2,2-disubstituted perhydrofuro[2,3-*b*]pyran derivatives using 2-*C*-branched (formylmethyl or acetylmethyl)-2-deoxy-D-glucosides as starting material has been developed. The strategy takes full advantage of the classical neighboring group participation phenomenon using carbonyl (formylmethyl or acetylmethyl) as the participating group to form the fused-ring products in good to excellent yield with excellent diastereoselectivity. Mechanistic studies demonstrated that the formation of 2,2-disubstituted perhydrofuro[2,3-*b*]pyrans from acetyl 2-*C*-acetylmethyl-2-deoxy-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside through a $S_N1$-type reaction to produce the pyran oxocarbenium ion, followed by intramolecular attack by the oxygen atom of ketone gave *cis*-5/6-fused ring oxocarbenium ions preferentially, which were further trapped by the nucleophiles from the less sterically hindered convex face to afford the products.

## Experimental section

### General information

All reactions sensitive to air or moisture were carried out under a nitrogen or argon atmosphere with anhydrous solvents. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Thin-layer

chromatography was performed using silica gel GF254 precoated plates (0.20–0.25 mm thickness) with a fluorescent indicator. Visualization on TLC was achieved by UV light (254 nm) and a typical TLC indication solution (10% sulfuric acid–ethanol solution). Column chromatography was performed on silica gel 90, 200–300 and 300–400 mesh. Optical rotations were measured with a Perkin Elmer M341 Digital Polarimeter. $^1$H and $^{13}$C NMR (600 and 150 MHz, respectively) spectra were recorded on a Bruker Avance 600 spectrometer. $^1$H NMR chemical shifts are reported in ppm ($\delta$) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, $\delta$ 7.26 ppm; $CD_3OD$, $\delta$ 3.31 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. $^{13}$C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, $\delta$ 77.0 ppm; $CD_3OD$, $\delta$ 49.0). ESI-HRMS spectra were recorded on BioTOFQ.

**(3a*R*,4*R*,5*S*,6*R*,7a*R*)-2-Acetoxyl-4,5-bis(benzyloxy)-6-[(benzyloxy)-methyl]-hexahydrofuro[2,3-*b*]pyran (6).** Methyl 2-*C*-formyl-methyl-2-deoxy-3,4,6-tri-*O*-benzyl-glucopyran **5** (0.9 g, 1.8 mmol) was dissolved in 34 mL HOAc, and 20 mL $Ac_2O$ was added. The mixture was cooled to 0 °C, and then 27 μL $H_2SO_4$ was added. The mixture was stirred at 0 °C until all of **5** disappeared (about 0.5 h). The reaction mixture was poured into ice water with vigorous stirring, and extracted with $CH_2Cl_2$ (20 mL × 3). The combined organic phase was washed successively with saturated $NaHCO_3$, saturated NaCl, and dried with $Na_2SO_4$. The crude product was purified by flash column chromatography.

Compound **6** obtained as colorless syrup; yield: 95%. $[\alpha]_D^{20}$ +67.5 (*c* 0.29, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.40–7.12 (m, 15H), 6.84 (t, *J* = 4.5 Hz, 1H), 6.34 (d, *J* = 3.2 Hz, 1H), 4.96 (d, *J* = 11.0 Hz, 1H), 4.83 (d, *J* = 10.7 Hz, 1H), 4.71 (d, *J* = 11.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 10.7 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 3.85–3.78 (m, 3H), 3.68 (d, *J* = 10.2 Hz, 2H), 2.30–2.23 (m, 1H), 2.21–2.16 (m, 1H), 2.12 (s, 3H), 1.97–1.93 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 168.8, 138.1, 138.1, 137.9, 128.5, 128.4, 128.0, 127.9, 127.9, 127.8, 127.8, 92.5, 89.5, 80.2, 79.0, 75.4, 75.0, 73.7, 73.1, 68.3, 40.3, 30.3, 20.9, 20.8; ESI-HRMS: *m*/*z* calcd for $C_{31}H_{34}NaO_7$ $[M + Na]^+$: 541.2204; found: 541.2204.

**Acetyl-2-*C*-acetonyl-2-deoxy-3,4,6-tri-*O*-benzyl-D-glucopyranoside (7).** Compound **7** was synthesized following a similar procedure to compound **6**, and obtained as colorless syrup; yield: 98%. $[\alpha]_D^{20}$ +79.5 (*c* 0.28, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.15 (m, 15H), 6.20 (d, *J* = 2.8 Hz, 1H), 4.95 (d, *J* = 11.3 Hz, 1H), 4.79 (d, *J* = 10.7 Hz, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 11.2 Hz, 1H), 4.59 (d, *J* = 10.7 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 3.86–3.85 (m, 1H), 3.84–3.81 (m, 1H), 3.80 (dd, *J* = 8.1, 2.9 Hz, 1H), 3.67 (dd, *J* = 11.0, 1.4 Hz, 1H), 3.64 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.64–2.54 (m, 2H), 2.26–2.14 (m, 1H), 2.08 (s, 3H), 2.04 (d, *J* = 7.7 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 206.1, 169.2, 138.2, 138.0, 137.9, 128.5, 128.4, 128.3, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 93.1, 79.9, 79.2, 75.0, 74.9, 73.6, 68.4, 41.2, 40.7, 29.8, 20.9; ESI-HRMS: *m*/*z* calcd for $C_{32}H_{36}NaO_7$ $[M + Na]^+$: 555.2359; found: 555.2349.

### General procedures for synthesis of 2-*C*-branched perhydrofuro[2,3-*b*]pyrans

To a stirring solution of **6** or **7** (0.1 mmol) in anhydrous $CH_3CN$ (1 mL) containing 100 mg of 4 Å M.S. at −40 °C and under a $N_2$ atmosphere was added nucleophiles (0.2 mmol). Then trimethylsilyl triflate (14.8 μL, 0.08 mmol) was added dropwise. The reaction mixture was stirred at −40 °C for 1.5 h, and then for 0.5 h at rt. The yellow mixture was diluted with $CH_2Cl_2$ (10 mL), and neutralized with a saturated $NaHCO_3$ solution (10 mL). The organic layer was collected, and the aqueous layer was re-extracted with further $CH_2Cl_2$ (2 × 10 mL). The combined organic phases were dried over anhydrous $Na_2SO_4$ and concentrated to give an orange syrup. The crude material was slightly diluted with $CH_2Cl_2$ (0.2 mL) and purified by silica gel flash column chromatography (petroleum ether–ethyl acetate, 8 : 1).

**(2*R*,3a*R*,4*R*,5*S*,6*R*,7a*R*)-2-Allyl-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-hexahydrofuro[2,3-*b*]pyran (8).** Obtained as a colorless syrup (39.2 mg, 78%); $[\alpha]_D^{20}$ +70.6 (*c* 0.30, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.19 (m, 15H), 5.80–5.67 (m, 1H), 5.45 (d, *J* = 4.5 Hz, 1H), 5.12–5.01 (m, 2H), 4.88 (d, *J* = 11.5 Hz, 1H), 4.78 (d, *J* = 10.9 Hz, 1H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.63 (d, *J* = 10.7 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.15 (dq, *J* = 12.0, 6.1 Hz, 1H), 3.82 (dd, *J* = 18.8, 7.9 Hz, 2H), 3.74 (t, *J* = 8.9 Hz, 1H), 3.70 (dd, *J* = 10.4, 1.4 Hz, 1H), 3.54 (t, *J* = 8.6 Hz, 1H), 2.32 (dt, *J* = 12.8, 6.4 Hz, 2H), 2.21 (dt, *J* = 13.4, 6.5 Hz, 1H), 1.88 (dd, *J* = 12.5, 5.8 Hz, 1H), 1.71–1.64 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 138.5, 138.3, 138.1, 133.9, 128.5, 128.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.6, 117.5, 101.5, 80.7, 77.9, 76.6, 74.6, 74.4, 73.6, 72.2, 68.8, 44.3, 40.7, 33.8; ESI-HRMS: *m*/*z* calcd for $C_{32}H_{36}NaO_5$ $[M + Na]^+$: 523.2460; found: 523.2455.

**(2*R*,3a*R*,4*R*,5*S*,6*R*,7a*R*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(2-methylallyl)-hexahydrofuro[2,3-*b*]pyran (10).** Obtained as a colorless syrup (43.7 mg, 85%); $[\alpha]_D^{20}$ +74.6 (*c* 0.30, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.37–7.20 (m, 15H), 5.46 (d, *J* = 4.6 Hz, 1H), 4.88 (d, *J* = 11.6 Hz, 1H), 4.79 (d, *J* = 11.2 Hz, 2H), 4.69 (d, *J* = 11.2 Hz, 2H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 10.8 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.23 (dq, *J* = 12.6, 6.3 Hz, 1H), 3.82 (dd, *J* = 15.5, 6.4 Hz, 2H), 3.75 (t, *J* = 8.9 Hz, 1H), 3.70 (d, *J* = 8.8 Hz, 1H), 3.54 (t, *J* = 8.6 Hz, 1H), 2.33 (dd, *J* = 13.9, 6.5 Hz, 2H), 2.08 (dd, *J* = 14.0, 6.4 Hz, 1H), 1.88 (dd, *J* = 12.8, 5.9 Hz, 1H), 1.70 (s, 3H), 1.68–1.62 (m, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 142.0, 138.5, 138.3, 138.1, 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.6, 112.6, 101.3, 80.6, 77.9, 75.8, 74.4, 74.4, 73.6, 72.2, 68.8, 44.8, 44.3, 34.4, 22.9; ESI-HRMS: *m*/*z* calcd for $C_{33}H_{38}NaO_5$ $[M + Na]^+$: 537.2617; found: 537.2621.

**(2*R*,3a*R*,4*R*,5*S*,6*R*,7a*S*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-cyano-hexahydrofuro[2,3-*b*]pyran (12).** Obtained as a colorless syrup (30.1 mg, 62%); $[\alpha]_D^{20}$ +85.1 (*c* 0.12, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.20 (m, 15H), 5.46 (d, *J* = 4.3 Hz, 1H), 4.92 (d, *J* = 11.7 Hz, 1H), 4.77 (d, *J* = 11.0 Hz, 1H), 4.69 (d,

$J$ = 11.7 Hz, 1H), 4.65 (dd, $J$ = 8.3, 2.8 Hz, 2H), 4.62 (d, $J$ = 4.2 Hz, 1H), 4.54 (d, $J$ = 12.1 Hz, 1H), 3.94 (d, $J$ = 9.2 Hz, 1H), 3.83 (dd, $J$ = 14.2, 5.9 Hz, 2H), 3.75 (d, $J$ = 8.9 Hz, 1H), 3.72 (d, $J$ = 10.4 Hz, 1H), 2.40–2.33 (m, 2H), 2.18 (d, $J$ = 13.8 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 138.2, 138.0, 137.9, 128.6, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 119.0, 103.3, 79.9, 77.4, 75.0, 74.4, 73.6, 72.9, 68.4, 63.0, 42.8, 32.8; ESI-HRMS: $m/z$ calcd for $C_{32}H_{31}NNaO_5$ $[M + Na]^+$: 508.2100; found: 508.2094.

**(2*S*,3*aR*,4*R*,5*S*,6*R*,7*aS*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-cyano-hexahydrofuro[2,3-*b*]pyran (13).** Obtained as a colorless syrup (11.6 mg, 24%); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.29 (m, 13H), 7.20 (d, $J$ = 7.3 Hz, 2H), 5.59 (d, $J$ = 4.7 Hz, 1H), 4.81 (d, $J$ = 11.9 Hz, 1H), 4.70 (d, $J$ = 11.1 Hz, 1H), 4.64–4.61 (m, 3H), 4.58–4.53 (m, 2H), 3.80 (d, $J$ = 9.1 Hz, 1H), 3.75 (dd, $J$ = 13.9, 10.0 Hz, 2H), 3.69–3.67 (m, 1H), 3.44 (t, $J$ = 7.3 Hz, 1H), 2.48 (s, 1H), 2.24 (dt, $J$ = 22.0, 7.5 Hz, 2H).

**(2*S*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-2-Allyl-4,5-bis(benzyloxy)-6-[(benzyloxy)-methyl]-2-methylhexahydrofuro[2,3-*b*]pyran (3).** Obtained as a colorless syrup (45.8 mg, 89%); $[\alpha]_D^{20}$ +46.2 ($c$ 0.41, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.41–7.29 (m, 15H), 5.88–5.77 (m, 1H), 5.50 (d, $J$ = 5.1 Hz, 1H), 5.12 (t, $J$ = 12.2 Hz, 2H), 4.83 (d, $J$ = 11.8 Hz, 1H), 4.75 (d, $J$ = 11.1 Hz, 1H), 4.69 (d, $J$ = 11.8 Hz, 1H), 4.68 (d, $J$ = 12.2 Hz, 1H), 4.58 (t, $J$ = 11.8 Hz, 2H), 3.95 (dt, $J$ = 8.9, 3.0 Hz, 1H), 3.82 (dd, $J$ = 10.7, 3.6 Hz, 1H), 3.79 (dd, $J$ = 8.9, 6.9 Hz, 1H), 3.74 (dd, $J$ = 10.6, 2.5 Hz, 1H), 3.70 (t, $J$ = 6.9 Hz, 1H), 2.49–2.42 (m, 1H), 2.30–2.21 (m, 2H), 2.01 (dd, $J$ = 13.3, 8.4 Hz, 1H), 1.77 (dd, $J$ = 13.3, 5.4 Hz, 1H), 1.29 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 138.4, 138.2(2), 128.4(2), 128.0, 127.9(2), 127.8(2), 127.6, 118.2, 100.6, 80.9, 80.2, 77.4, 73.7, 73.5, 73.3, 71.9, 69.2, 47.0, 43.9, 38.0, 27.7; ESI-HRMS: $m/z$ calcd for $C_{33}H_{38}NaO_5$ $[M + Na]^+$: 537.2617; found: 537.2611.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-methyl-2-(2-methylallyl)-hexahydrofuro[2,3-*b*]pyran (14).** Obtained as a colorless syrup (42.8 mg, 81%); $[\alpha]_D^{20}$ +52.1 ($c$ 0.17, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.37–7.19 (m, 19H), 5.44 (d, $J$ = 5.1 Hz, 1H), 4.86 (s, 1H), 4.78 (d, $J$ = 11.8 Hz, 1H), 4.70 (d, $J$ = 11.4 Hz, 2H), 4.64 (d, $J$ = 11.8 Hz, 1H), 4.64 (d, $J$ = 12.1 Hz, 1H), 4.54 (d, $J$ = 12.1 Hz, 1H), 4.52 (d, $J$ = 12.6 Hz, 1H), 3.89 (dt, $J$ = 8.9, 2.9 Hz, 1H), 3.79–3.73 (m, 2H), 3.70 (dd, $J$ = 10.6, 2.5 Hz, 1H), 3.66 (t, $J$ = 6.8 Hz, 1H), 2.42 (dd, $J$ = 13.5, 6.4 Hz, 1H), 2.20 (d, $J$ = 13.5 Hz, 1H), 2.13 (d, $J$ = 13.4 Hz, 1H), 2.05–2.00 (m, 1H), 1.80 (s, 3H), 1.76 (dd, $J$ = 13.2, 5.6 Hz, 1H), 1.26 (s, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 142.7, 138.5, 138.2, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 114.7, 100.5, 81.5, 80.1, 76.8, 73.7, 73.5, 73.3, 71.9, 69.2, 49.9, 43.8, 38.9, 27.8, 24.3; ESI-HRMS: $m/z$ calcd for $C_{34}H_{40}NaO_5$ $[M + Na]^+$: 551.2773; found: 551.2768.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-2-[(Benzoyl)methyl]-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-methyl-hexahydro-furo[2,3-*b*]pyran (16).** Colorless syrup, 54.5 mg, yield: 92%, $[\alpha]_D^{20}$ +30.1 ($c$ 0.25, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.95 (d, $J$ = 7.4 Hz, 2H), 7.56 (t, $J$ = 7.4 Hz, 1H), 7.45 (t, $J$ = 7.7 Hz, 2H), 7.37–7.27 (m, 13H), 7.20 (d, $J$ = 6.5 Hz, 2H), 5.41 (d, $J$ = 5.1 Hz, 1H), 4.74 (d, $J$ = 11.6 Hz, 1H), 4.68 (d, $J$ = 11.1 Hz, 1H), 4.64 (d, $J$ = 11.7 Hz, 1H), 4.61 (d, $J$ = 12.1 Hz, 1H), 4.52 (d, $J$ = 11.0 Hz, 1H), 4.51 (d, $J$ = 12.2 Hz, 1H), 3.89 (dt, $J$ = 8.5, 3.0 Hz, 1H), 3.78–3.70 (m, 2H), 3.68 (dd, $J$ = 8.2, 4.8 Hz, 2H), 3.19 (d, $J$ = 2.5 Hz, 2H), 2.47–2.41 (m, 1H), 2.34 (dd, $J$ = 13.6, 8.4 Hz, 1H), 2.02 (dd, $J$ = 13.6, 5.8 Hz, 1H), 1.44 (s, 3H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 198.6, 138.3, 138.2, 138.1, 137.5, 133.2, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.8, 127.6, 100.5, 80.8, 79.8, 77.1, 73.6, 73.5, 73.2, 72.0, 69.2, 49.7, 43.6, 38.4, 28.6. ESI-HRMS: $m/z$ calcd for $C_{38}H_{40}NaO_6$ $[M + Na]^+$: 615.2717; found: 615.2717.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(1-cyclohexanon-2-yl)-2-methylhexahydro-furo[2,3-*b*]pyran (18).** Colorless syrup, 54.2 mg, yield: 95%, $[\alpha]_D^{20}$ +75.9 ($c$ 0.48, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.20 (m, 15H), 5.41 (dd, $J$ = 7.4, 5.2 Hz, 1H), 4.81 (dd, $J$ = 11.5, 3.5 Hz, 1H), 4.78–4.72 (m, 1H), 4.69 (t, $J$ = 11.2 Hz, 1H), 4.63 (d, $J$ = 12.2 Hz, 1H), 4.58 (dd, $J$ = 14.3, 11.2 Hz, 1H), 4.54 (d, $J$ = 12.2 Hz, 1H), 3.90 (dd, $J$ = 12.5, 5.8 Hz, 1H), 3.79 (td, $J$ = 10.3, 3.4 Hz, 1H), 3.74–3.66 (m, 3H), 2.53 (ddd, $J$ = 57.9, 12.6, 4.7 Hz, 1H), 2.41–2.25 (m, 4H), 2.13–1.99 (m, 3H), 1.93 (s, 1H), 1.71–1.55 (m, 3H), 1.40 (s, 1H), 1.30 (s, 1H), 1.26 (dd, $J$ = 8.4, 5.8 Hz, 1H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 211.6, 211.5, 138.4, 138.4, 138.2, 138.2, 138.1, 128.5, 128.4, 128.4, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.6, 101.6, 100.5, 82.1, 81.4, 81.2, 80.7, 77.6, 74.2, 74.0, 73.9, 73.6, 72.1, 69.1, 69.0, 62.2, 60.6, 44.6, 44.0, 43.5, 43.4, 40.3, 36.1, 29.3, 29.2, 28.9, 28.3, 28.1, 25.4, 25.3, 23.6. ESI-HRMS: $m/z$ calcd for $C_{36}H_{42}NaO_6$ $[M + Na]^+$: 593.2874; found: 593.2870.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-[(2,2-dimethyl-propionyl)methyl]-2-methylhexahydrofuro[2,3-*b*]-pyran (20).** Colorless syrup, 49.2 mg, yield: 86%, $[\alpha]_D^{20}$ +68.7 ($c$ 0.42, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.37–7.20 (m, 15H), 5.46 (d, $J$ = 5.0 Hz, 1H), 4.78 (d, $J$ = 11.5 Hz, 1H), 4.72 (d, $J$ = 11.1 Hz, 1H), 4.67 (d, $J$ = 11.5 Hz, 1H), 4.63 (d, $J$ = 12.1 Hz, 1H), 4.56 (d, $J$ = 11.3 Hz, 1H), 4.53 (d, $J$ = 12.3 Hz, 1H), 3.90 (dd, $J$ = 6.2, 2.7 Hz, 1H), 3.78 (dd, $J$ = 10.6, 3.6 Hz, 1H), 3.76–3.72 (m, 1H), 3.72–3.66 (m, 2H), 2.84 (d, $J$ = 17.4 Hz, 1H), 2.68 (d, $J$ = 17.4 Hz, 1H), 2.44–2.37 (m, 1H), 2.25 (dd, $J$ = 13.8, 8.3 Hz, 1H), 2.01 (dd, $J$ = 13.8, 4.9 Hz, 1H), 1.36 (s, 3H), 1.12 (s, 9H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 214.2, 138.3, 138.2, 128.5, 128.4, 128.4, 128.0, 127.9, 127.9, 127.8, 127.8, 127.6, 100.5, 80.3, 80.2, 77.4, 73.8, 73.5, 73.5, 72.1, 69.1, 47.8, 44.7, 43.9, 38.9, 27.9, 26.2. ESI-HRMS: $m/z$ calcd for $C_{36}H_{44}NaO_6$ $[M + Na]^+$: 595.3030; found: 595.3049.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-2-[(Acetyl)methyl]-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-methylhexahydrofuro[2,3-*b*]pyran (22).** Colorless syrup, 47.8 mg, yield: 95%, $[\alpha]_D^{20}$ +43.1 ($c$ 0.54, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.37–7.20 (m, 15H), 5.47 (d, $J$ = 5.1 Hz, 1H), 4.77 (d, $J$ = 11.8 Hz, 1H), 4.70 (d, $J$ = 11.1 Hz, 1H), 4.64 (t, $J$ = 11.8 Hz, 2H), 4.54 (d, $J$ = 11.0 Hz, 2H), 4.53 (d, $J$ = 12.1 Hz, 1H), 3.89 (dt, $J$ = 8.6, 3.0 Hz, 1H), 3.77 (dd, $J$ = 10.7, 3.8 Hz, 1H), 3.75–3.72 (m, 1H), 3.70 (dd, $J$ = 10.7, 2.5 Hz, 1H), 3.66 (t, $J$ = 6.7 Hz, 1H), 2.66 (d, $J$ = 14.9 Hz, 1H), 2.56 (d, $J$ = 14.9 Hz, 1H), 2.46–2.40 (m, 1H), 2.17 (s, 3H), 2.14 (dd, $J$ = 13.6, 8.4 Hz, 1H), 1.90 (dd, $J$ = 13.6, 5.6 Hz, 1H), 1.34 (s, 3H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 207.4, 138.3, 138.1, 138.1, 128.5, 128.4, 128.4, 128.1, 127.9, 127.9, 127.9, 127.8, 127.6, 100.6, 79.9, 79.8, 77.1, 73.7, 73.5, 73.3, 72.0, 69.1, 54.8,

43.6, 38.8, 31.9, 28.0. ESI-HRMS: *m*/*z* calcd for $C_{33}H_{38}NaO_6$ $[M + Na]^+$: 553.2551; found: 553.2561.

**(2*R*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-cyano-2-methylhexahydrofuro[2,3-*b*]pyran (23).** Colorless syrup, 25.3 mg, yield: 58%, $[\alpha]_D^{20}$ +49.5 (*c* 0.69, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.40–7.27 (m, 14H), 7.23–7.19 (m, 2H), 5.60 (d, *J* = 5.5 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 4.65–4.59 (m, 3H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.50 (d, *J* = 11.2 Hz, 1H), 3.84–3.80 (m, 1H), 3.76–3.70 (m, 2H), 3.68 (dd, *J* = 10.7, 2.6 Hz, 1H), 3.53 (t, *J* = 5.8 Hz, 1H), 2.68–2.60 (m, 1H), 2.41 (dd, *J* = 13.7, 8.1 Hz, 1H), 1.95 (dd, *J* = 13.7, 7.2 Hz, 1H), 1.56 (s, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 138.0, 137.9, 137.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.9, 127.7, 121.2, 101.6, 77.5, 76.4, 73.5, 73.4, 72.7, 72.7, 72.3, 69.0, 41.6, 39.8, 26.3; ESI-HRMS: *m*/*z* calcd for $C_{31}H_{33}NNaO_5$ $[M + Na]^+$: 522.2251; found: 522.2256.

**(2*S*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-Bis(benzyloxy)-6-[(benzyloxy)methyl]-2-cyano-2-methylhexahydrofuro[2,3-*b*]pyran (24).** Colorless syrup, 14 mg, yield: 32%, $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.36–7.27 (m, 13H), 7.22 (d, *J* = 6.7 Hz, 2H), 5.51 (d, *J* = 4.6 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.78 (d, *J* = 11.1 Hz, 1H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.64 (d, *J* = 12.9 Hz, 1H), 4.62 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.27–4.25 (m, 1H), 3.97–3.94 (m, 2H), 3.82 (dd, *J* = 10.8, 3.2 Hz, 1H), 3.75–3.69 (m, 2H), 2.43–2.37 (m, 1H), 2.10 (dd, *J* = 6.8, 2.8 Hz, 1H), 2.04 (dd, *J* = 14.8, 8.0 Hz, 1H), 1.61 (s, 3H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 138.3, 138.0, 137.9, 128.7, 128.6, 128.5, 128.4, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 121.6, 102.6, 80.2, 77.6, 75.1, 74.4, 73.6, 72.9, 72.6, 68.4, 44.7, 40.8, 28.3. ESI-HRMS: *m*/*z* calcd for $C_{31}H_{33}NNaO_5$ $[M + Na]^+$: 522.2251; found: 522.2271.

**Synthesis of (2*S*,3*aR*,4*R*,5*S*,6*R*,7*aR*)-4,5-dihydroxy-6-(hydroxymethyl)-2-methyl-2-propanyl-hexahydrofuro[2,3-*b*]pyran (25).** To a solution of **3** (0.26 g, 0.51 mmol) in MeOH (10 mL) were added 10% Pd-C (0.026 g) and HCOOH (0.5 mL). The mixture was stirred at 50 °C under an atmosphere of $H_2$ overnight. The mixture was cooled to room temperature, filtered over diatomaceous earth, and concentrated *in vacuo*, purified by silica gel flash column chromatography (ethyl acetate–MeOH = 20 : 1) to afford compound **25** (0.11 g, 0.46 mmol, 90%) as a colourless solid; $[\alpha]_D^{20}$ +30.9 (*c* 0.14, $CHCl_3$); $^1$H NMR (600 MHz, MeOH-$d_4$): $\delta$ 5.36 (d, *J* = 4.5 Hz, 1H), 3.78 (dd, *J* = 11.9, 2.6 Hz, 1H), 3.74 (dd, *J* = 11.9, 4.9 Hz, 1H), 3.64 (ddd, *J* = 9.4, 4.8, 2.6 Hz, 1H), 3.56 (t, *J* = 8.8 Hz, 1H), 3.35 (t, *J* = 9.1 Hz, 1H), 2.10–2.05 (m, 1H), 2.02 (dd, *J* = 13.1, 7.6 Hz, 1H), 1.97 (dd, *J* = 13.2, 2.2 Hz, 1H), 1.49 (ddd, *J* = 16.3, 11.0, 4.8 Hz, 2H), 1.39 (ddd, *J* = 16.4, 12.2, 6.2 Hz, 2H), 1.35 (s, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (150 MHz, MeOH-$d_4$): $\delta$ 100.8, 80.5, 74.5, 74.0, 69.9, 61.3, 45.3, 45.2, 38.5, 26.5, 17.3, 13.5; ESI-HRMS: *m*/*z* calcd for $C_{12}H_{22}NaO_5$[M + Na]$^+$: 269.1359 found: 269.1362.

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