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# Divergent syntheses of all 16 carbasugar stereoisomers via stereoconversion of carba-β-D-altropyranose derivatives

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**Abstract**—We have developed practical synthetic routes to enantiopure D- and L-carba-β-altrose derivatives and all the possible stereoisomers via their divergent stereoconversions. Carba-β-D-altrose was prepared from 3-cyclohexene-1-carboxylic acid and converted to carba-β-D-mannose, carba-β-D-idose, and carba-β-D-talose derivatives via regio- and stereoselective oxidation/reduction of 3-OH and/or 4-OH. The four carbasugar stereoisomers were then transformed to the remaining 12 carbasugar stereoisomers and their 1,2-epoxides by regio- and stereoselective manipulation of hydroxyl groups in C1 and C2, which includes oxidation/reduction, Mitsunobu's reaction, olefination/dihydroxylation, and epoxidation/ring-opening protocols.
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## 1. Introduction

Recent glycobiology studies have revealed the versatile and critical roles of cell-surface carbohydrates in the recognition processes of cells via carbohydrate–protein interactions, which eventually result in cell adhesion, cell growth, immune response, fertilization, viral infection, inflammation, metastasis of cancer, etc.[1] The major issues in glycobiology now are the understanding at the molecular level of the carbohydrate–protein interactions in pathophysiologically important processes, and how to efficiently develop molecular tools that can regulate such carbohydrate–protein interactions, thus leading to therapies. In this context, much of the research has been focused on developing glycomimetic molecules both as biochemical probes and potential drug candidates.[2] These research efforts require diverse structures of carbohydrate mimetics, among which non-hydrolyzable analogues[3] are thought to be highly desirable because of their stability in vivo.

Carbasugars are suitable building blocks for non-hydrolyzable carbohydrate mimetics due to their structural resemblance to cyclic monosaccharides and inherent stability to glycosidases. Ogawa et al. have provided the early leading role in this area and have synthesized a number of carbasugars, including disaccharide and trisaccharide analogues as glycosidase inhibitors or glycosyltransferase inhibitors.[3a,c,d,4] They also synthesized some carbasugar analogues of glycosylceramide as potential ceramide glycosyltransferase inhibitors.[5] Other groups have also investigated carbasugar nucleotide analogues as glycosyltransferase inhibitors.[6]

Application of carbasugars to diverse carbohydrate mimetics is still limited because of the paucity of readily available carbasugars as building block. To be widely used as diverse carbohydrate mimetics, all required carbasugars such as enantiopure stereoisomers of carbasugars as *glycosyl acceptor mimics* and their 1,2-epoxide derivatives as *glycosyl donor mimics* should be made available by practical routes. In addition, the available building blocks of 16(32) of possible stereoisomers and 8(16) of possible 1,2-epoxides should be appropriately protected for further synthetic elaborations. Although a variety of synthetic methods[3a–h,7] have been developed for carbasugars since the pioneering work by McCasland et al. in 1966,[8] there are no general and practical synthetic routes defined for ready access to the carbasugar building blocks.

Recently, we have investigated practical synthetic routes to all 16 enantiopure carbasugar analogues for α- and β-aldohexopyranose stereoisomers and their 1,2-epoxide derivatives. We imagined that *systematic stereochemical manipulation of one carbasugar to other stereoisomers* might be more practical in obtaining all the desired

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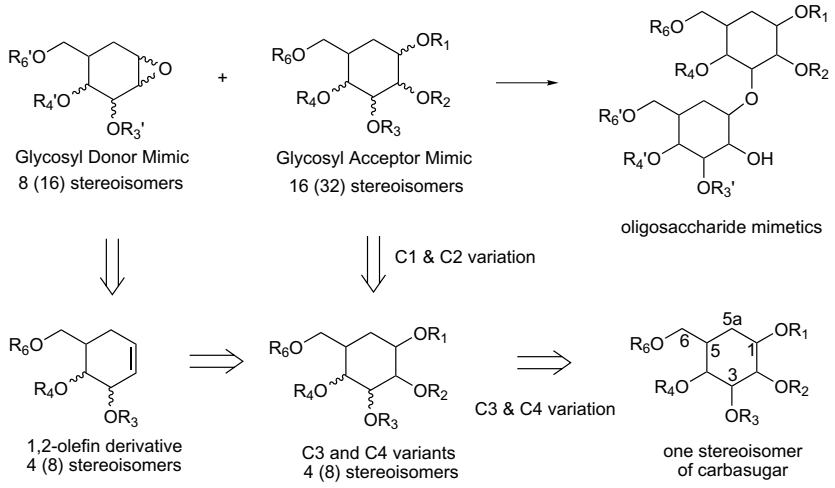



**Figure 1.**

carbasugar stereoisomers rather than using multiple synthetic routes for each stereoisomer. It was envisioned that a series of operations involving (1) the synthesis of *a suitable carbasugar stereoisomer* in enantiopure form (both of D- and L-form), followed by (2) conversion to its 'C3 and C4 stereo-variants', and then (3) conversion of the resulting four (eight) stereoisomers to their 1,2-epoxides and 12 more stereoisomers might provide practical synthetic routes to all stereoisomeric carbasugar building blocks (Fig. 1). This stereoconversion strategy may have some advantages. First, since all stereoisomers can be obtained from one key intermediate, only one resolution on a practical scale is necessary. Second, a limited set of orthogonal protecting groups for various hydroxyl groups can be utilized in a number of stereoselective manipulations throughout the stereoconversion strategy.

The initial challenges in these conversion strategies included the practical supply of a suitable enantiopure stereoisomer and regio- and stereo-selective manipulations of various hydroxyl groups of carbasugars. We previously reported in a preliminary fashion a practical synthesis of enantiopure D- and L- of carba-β-altropyranose derivatives and their straightforward stereoconversions to carba-β-mannopyranose, carba-β-idopyranose, and carba-β-talopyranose derivatives as 'C3 and C4 stereo-variants'.[9] We herein report the successful development of *C1 and/or C2 stereoconversion routes* from the four 'C3 and C4 stereo-variants' to the remaining 12 stereoisomers of all 16 carbasugars (D-forms only) as well as some of their 1,2-epoxide derivatives.

## 2. Results and discussion

*General strategy*. The D- and L- of carba-β-altropyranose derivatives have been synthesized from commercially available 3-cyclohexene-1-carboxylic acid via sequential and stereoselective introductions of necessary hydroxyl groups combined with an efficient enzymatic resolution. The C3 and C4 variants of carba-β-altropyranose, that is, carba-β-mannopyranose, carba-β-idopyranose, and, carba-β-talopyranose derivatives, have been synthesized via procedures involving regioselective benzoylation and stereoselective oxidation/reduction (Fig. 2).[9] For the syntheses of the remaining 12 stereoisomers (D-forms only) and their 1,2-epoxide derivatives, we used suitable stereo-inversion methods for C1 and C2 of the four stereoisomers D-**2a**, D-**3a**, D-**4a**, and

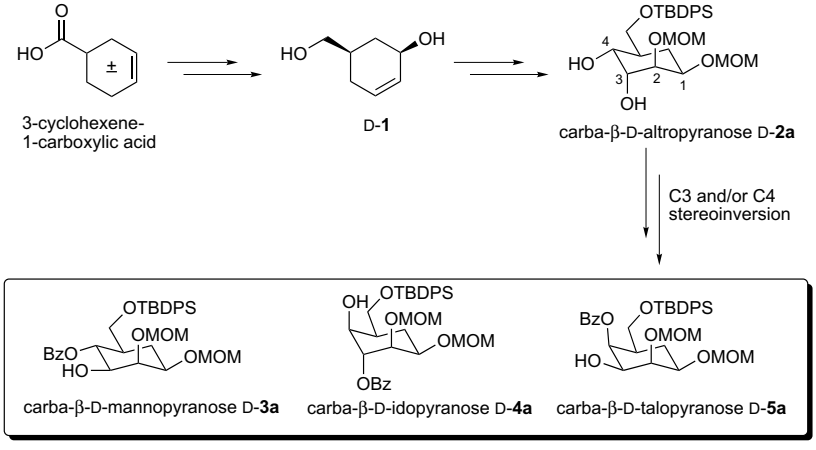



**Figure 2.**

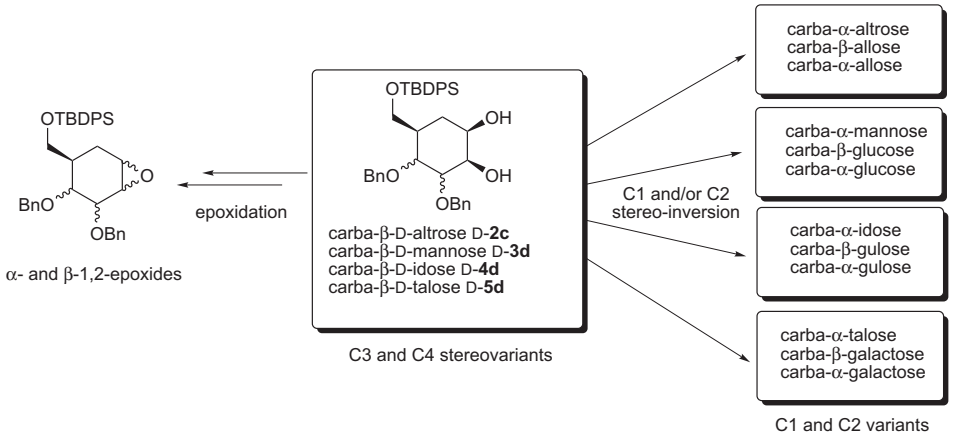


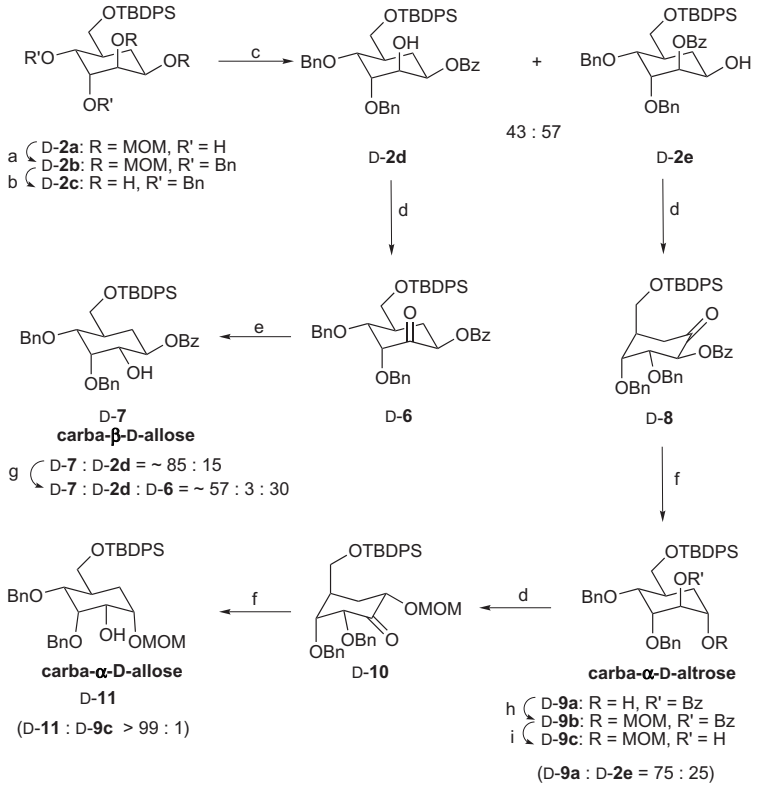

**Figure 3.**

D-**5a** depending on their stereochemistry at C3 and C4. First, each 1,2-diol derivative of the 'C3 and C4 stereovariants' was prepared by protecting the C3 and C4 hydroxyl groups as benzyl ether and subsequently removing the MOM groups in D-**2a**, D-**3a**, D-**4a**, and D-**5a**.

These four *cis*-1,2-diols were subjected to either an oxidation/reduction, a Mitsunobu reaction, olefination/dihydroxylation, or epoxidation/ring-opening procedures as deemed necessary. During the stereoconversions of those four carbasugar stereoisomers, several α- and β-1,2-epoxide derivatives were also synthesized by the epoxidation of 1,2-olefin derivatives, while some of the β-1,2-epoxide derivatives were stereoselectively synthesized via bromoacetoxy intermediates that were easily derived from the 1,2-diol derivatives (Fig. 3).

## 2.1. Transformation of carba-β-D-altropyranose to carba-α-D-altropyranose, carba-β-D-allopyranose, and carba-α-D-allopyranose derivatives

Syntheses of carba-α-D-altrose, carba-α-D-allose, and carba-β-D-allose derivatives were accomplished by regioselective protection and oxidation/reduction of 1-OH and 2-OH of carba-β-D-altrose derivatives (Scheme 1). After protection of 3- and 4-OH of




**Scheme 1.** Reagents and conditions: (a) NaH (4 equiv), BnBr (4 equiv), $Bu_4NI$ (0.2 equiv), THF, rt, 90%; (b) TMSBr (10 equiv), molecular sieve 4 Å, $CH_2Cl_2$, −20 °C, 64%; (c) (i) $(EtO)_3CPh$ (2 equiv), TSA (0.1 equiv), $CH_2Cl_2$, rt, (ii) 80% aq AcOH, 95%; (d) PCC (3 equiv), molecular sieves 4 Å, $CH_2Cl_2$, rt, D-**2d** or reflux, D-**2e**; (e) $BH_3{\cdot}Me_2S$ (5 equiv), THF, 0 °C; (f) $NaBH_4$ (5.0 equiv), MeOH (50 equiv), $CH_2Cl_2$, 0 °C; (g) PCC (3.0 equiv), molecular sieves 4 Å, $CH_2Cl_2$, rt, 2 h; (h) MOMCl (10 equiv), $(i\text{-}Pr)_2NEt$ (10 equiv), $CH_2Cl_2$, reflux, 15 h, 84%; (i) NaOMe (5 equiv), MeOH, rt, 14 h.

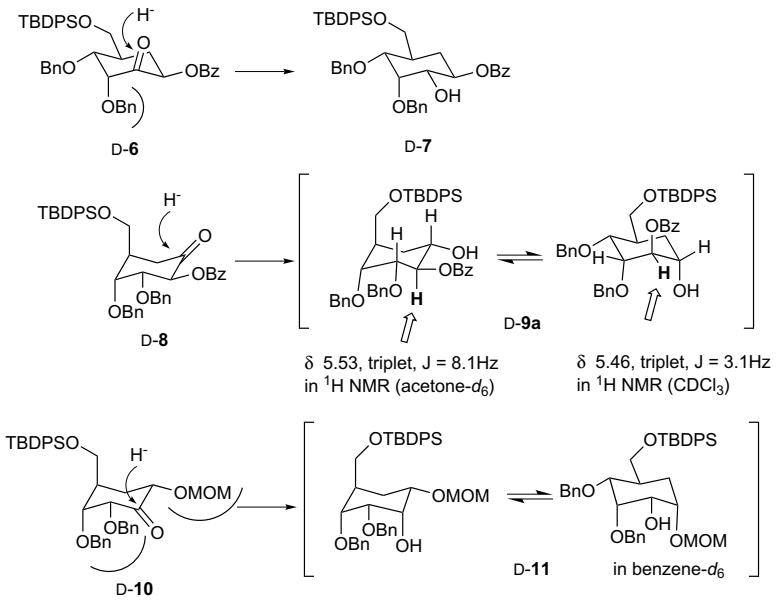



**Figure 4.**

carba-β-D-altrose D-**2a** as benzyl ethers by treatment with NaH, BnBr, and $Bu_4NI$,[10] subsequent deprotection of the MOM groups with TMSBr[11] gave carba-β-D-altrose 1,2-diol derivative D-**2c**. Treatment of this diol D-**2c** with triethyl orthobenzoate and TSA, followed by hydrolysis in 80% aq AcOH,[12] gave a mixture of monobenzoates (D-**2d**/D-**2e** = 43:57). Oxidation of D-**2d** with PCC[3c,13] gave the 2-keto derivative D-**6**, which was reduced with $NaBH_4$ to give a mixture of carba-β-allose derivatives D-**7** and D-**2d** (D-**7**/D-**2d** = ~80:20). As D-**7** and D-**2d** were not easily separable, attempts were made to enhance the selectivity for D-**7** with other reducing agents with no satisfactory results (D-**7**/D-**2d** ~ 85:15 by $BH_3{\cdot}Me_2S$, THF, ~75:25 by $NaBH_4$, $CeCl_3$).[3d] However, it was found that the oxidation rate of 2-OH (axial) in D-**2d** was much faster than that of 2-OH (equatorial) in D-**7**.[14] Thus, a preferential oxidation of D-**2d** in the mixture (D-**7**/D-**2d** = 85:15 by $BH_3{\cdot}Me_2S$) was carried out with PCC (3.0 equiv) for 2 h at rt, which resulted carba-β-D-allose derivative D-**7** in good diastereomeric purity (D-**7**, 90% de, 60%) and the 2-keto compound (D-**6**, 30%).

Oxidation of D-**2e** with PCC gave 1-keto derivative D-**8**, which upon reduction gave a mixture of carba-α-altrose derivatives D-**9a** and D-**2e** (75:25 with $NaBH_4$, $CH_2Cl_2$/MeOH, or $BH_3{\cdot}Me_2S$ in THF). Although the stereoselectivity in this reduction was not very high, the mixture was readily separable to provide diastereomerically pure carba-α-D-altrose derivative D-**9a** (69%). Protection of the 1-OH of D-**9a** as the MOM ether[15] and subsequent removal of the benzoyl group gave D-**9c** in good yield. A similar oxidation (PCC)/reduction ($NaBH_4$) protocol transformed the D-**9c** to a carba-α-D-allose derivative D-**11** with high stereoselectivity (D-**11**/D-**9c** = >99:1).

$NaBH_4$ reductions of cyclohexanone derivatives with well-defined chair conformations are generally known to give equatorial alcohol as the major product (equatorial:axial = ca. 8:2–9:1) via axial attack of the hydride.[16] This preference for equatorial alcohol can be enhanced or diminished depending on the neighboring groups present in the ketone. In many reported cases, the benzyloxy group seems to provide substantial steric hindrance to the axial approach of the hydride to the carbonyl group, while the benzoate group does not.[9,17] In the reduction of D-**6**, the preference for equatorial alcohol was expected to be increased by the 3-OBn group, which might hinder the bottom side approach of the hydride, while the observed ratio was 4:1 (D-**7**/D-**2d**). In the reduction of D-**8**, a similar preference for equatorial alcohol was expected to give D-**9a** as the major product (Fig. 4). However, the axial $TBDPSOCH_2$ group appeared to cause some steric hindrance to the topside approach of the hydride, thus decreasing the preference for D-**9a** to a degree. Interestingly, D-**9a** shows two different conformations depending on the solvents. In the $^1H$ NMR of D-**9a**, while a small coupling constant of H-2 peak (t, $J = 3.1$ Hz) supports a conventional chair conformation in which the $TBDPSOCH_2$ group has equatorial orientation, the relatively large coupling constant of H-2 peak (t, $J = 8.1$ Hz) in acetone-$d_6$ suggests a flipped chair conformer as shown in Figure 4. In the reduction of D-**10**, the preference for equatorial –OH is completely negated by the serious neighboring group effects (1-OMOM, 3- and 4-OBn groups) to give D-**11** exclusively. The coupling relationships in compounds D-**2**–D-**11** are summarized in Table 1.

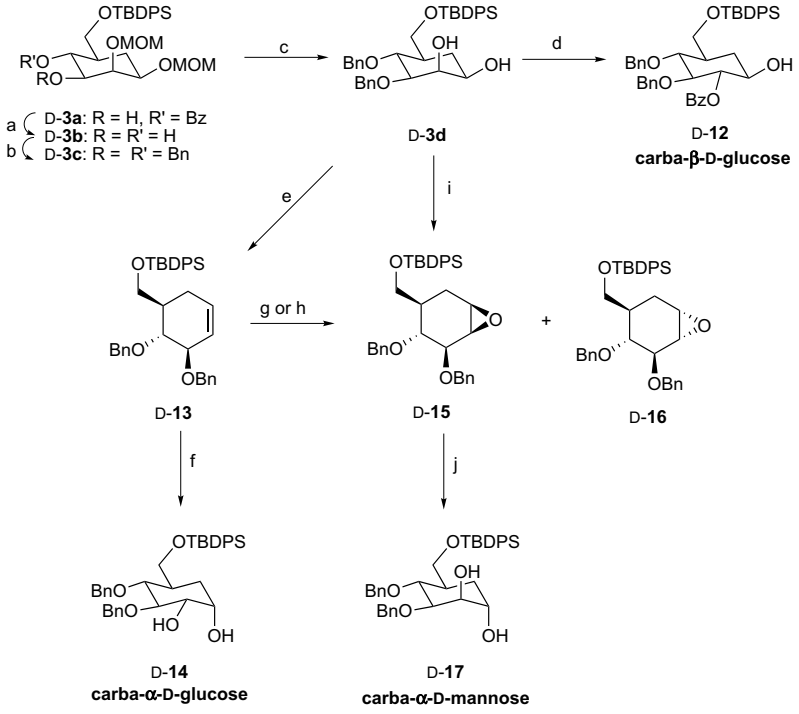
### 2.2. Transformation of carba-β-D-mannopyranose to carba-α-D-mannopyranose, carba-β-D-glucopyranose, and carba-α-D-glucopyranose derivatives

Adjusting the stereochemistry of C1 and/or C2 of the carba-β-mannose derivative D-**3a** gave carba-β-glucose D-**12**, carba-α-glucose D-**14**, and carba-α-mannose D-**17** derivatives (Scheme 2). Due to the opposite stereochem-

**Table 1.**

| Compd | Coupling constants (Hz) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $J_{H1-H2}$ | $J_{H2-H3}$ | $J_{H3-H4}$ | $J_{H4-H5}$ | $J_{H5-H5a\alpha}$ | $J_{H5-H5a\beta}$ | $J_{H1-H5a\alpha}$ | $J_{H1-H5a\beta}$ |
| D-**2d**[a] | 3.6 | 3.6 | nd | nd | 4.3 | 12.2 | 4.3 | 12.2 |
| D-**2e**[a] | Small | Small | 2.6 | 10.4 | nd | 12.0 | nd | 12.0 |
| D-**6**[a] | — | — | 2.7 | 10.7 | 4.1 | 12.9 | 6.9 | 13.0 |
| D-**7**[a] | 9.7 | Singlet | 2.6 | 9.8 | nd | nd | 5.1 | 11.3 |
| D-**8**[a] | — | 9.7 | 2.6 | 3.3 | 6.8 | Small | — | — |
| D-**9a**[a] | 3.2 | 2.9 | 2.9 | 9.9 | nd | 13.5 | Small | 2.9 |
| D-**9b**[a] | 7.8 | 7.8 | 2.7 | 4.9 | nd | nd | 8.5 | 4.6 |
| D-**9c**[b] | 9.3 | 9.3 | 2.6 | 2.6 | 5.8 | nd | 12.5 | nd |
| D-**10**[a] | — | — | Small | Small | 6.0 | Small | 12.1 | 7.2 |
| D-**11**[b] | Small | Small | 2.2 | 9.1 | 4.7 | 10.4 | 4.7 | 3.2 |

—: No vicinal proton pair exist.
Small: assumed from broad singlet.
nd: not determined.
[a] In $CDCl_3$.
[b] In $C_6D_6$.




**Scheme 2.** Reagents and conditions: (a) NaOMe (0.1 equiv), MeOH, rt, 2 h, 92%; (b) NaH (4 equiv), BnBr (4 equiv), $Bu_4NI$ (0.2 equiv), THF, rt, 81%; (c) TMSBr (10 equiv), molecular sieves 4 Å, $CH_2Cl_2$, −20 °C, 78%; (d) $PPh_3$, DEAD, BzOH, toluene, reflux, 63%; (e) $PPh_3$, imidazole, $I_2$, toluene, reflux, 90%; (f) $OsO_4$ (cat.), NMO (2 equiv), acetone/water (8:1), rt, quantitative; (g) *m*-CPBA, D-**15**/D-**16** = 1:4; (h) (i) NBS (or NIS), dioxane/water (10:1), (ii) NaOMe/MeOH, D-**15**/D-**16** = 1:4 (1:10 for NIS); (i) (i) $(CH_3O)_3CCH_3$ (1.5 equiv), PPTS, $CH_2Cl_2$, (ii) AcBr (3.0 equiv), $Et_3N$ (0.1 equiv), $CH_2Cl_2$, (iii) NaOMe/MeOH, only D-**15** was formed, 95%; (j) $HClO_4$ (3% in water, 0.4 equiv), acetone, 0 °C, 95%.

istry of C3 in D-**3a** compared to carba-β-altrose D-**2a**, oxidation/reduction of 1- and/or 2-OH in carba-β-mannose derivatives was not expected as a suitable protocol to produce the other stereoisomers. Thus, we used alternative strategies employing a Mitsunobu reaction, didehydroxylation/dihydroxylation, and epoxidation/ring-opening to obtain the desired stereoisomers. The 1,2-diol D-**3d** was prepared by conventional protection and deprotection of D-**3a**. Mitsunobu reaction[18] of D-**3d** with $PPh_3$, DEAD, and BzOH gave carba-β-D-glucose derivative D-**12** with inversion of only the axial –OH at C2. The three proton peaks appear in the $^1H$ NMR as triplets at $\delta = 3.69$, 3.75, and 5.24 ppm each with $J = 9.2$, 9.3, and 9.3 Hz in acetone-$d_6$, indicating that H1, H2, H3, and H4 have all axial orientations. Didehydroxylation of D-**3d** was successfully accomplished by a modified 'Samuelsson's procedure'.[19] A preliminary reaction of D-**3d** with $PPh_3$ (4 equiv), imidazole (4 equiv), and $I_2$ (3.3 equiv) gave D-**13** in a low yield together with complex by-products. However, the use of a larger excess amount of imidazole ($PPh_3$/imidazole/$I_2$ = 4:8:3.3 equiv) was found to give the 1,2-olefin derivative

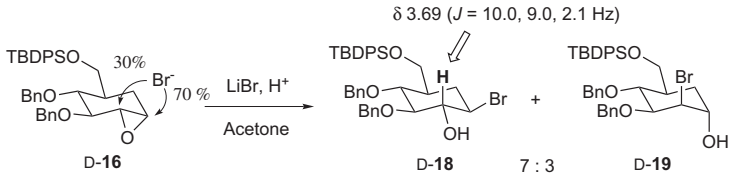



**Figure 5.**

D-**13** cleanly in a good yield. Subsequent dihydroxylation of D-**13** with a catalytic amount of $OsO_4$[20] and an excess NMO gave carba-α-D-glucose derivative D-**14** as the sole product in quantitative yield. The coupling constants of H1 (app q, $J = 2.5$ Hz) and H2 (dd, $J = 9.2$, 2.8 Hz) in the $^1$H NMR spectrum of D-**14** are in good agreement with its structure.

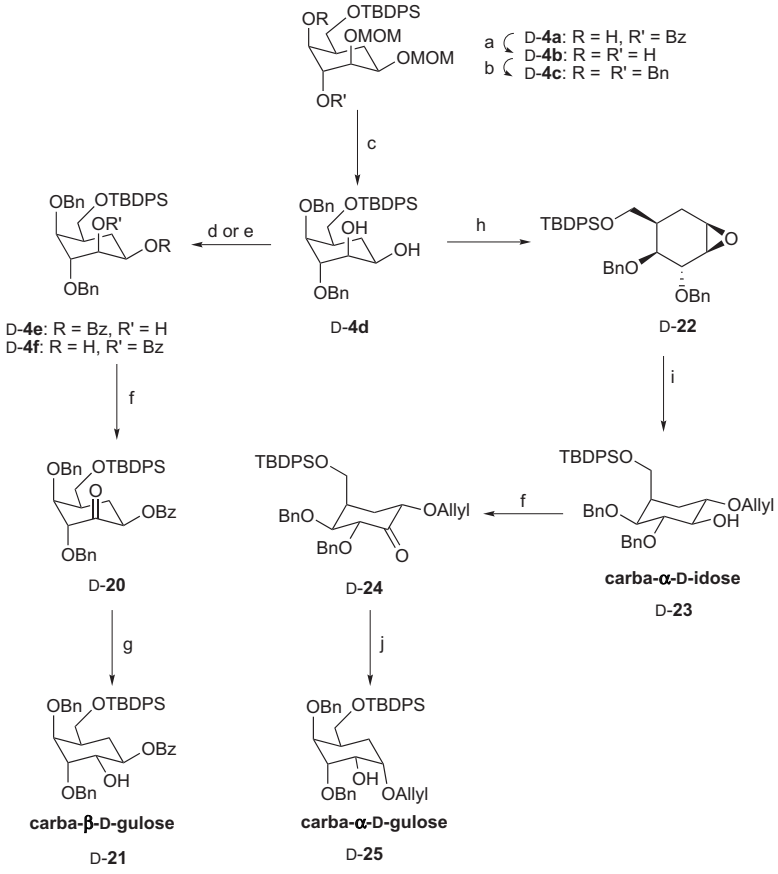
Several epoxidation conditions were examined on D-**13** for its stereoselective conversion to the α- or β-1,2-epoxide derivatives. Treatment of D-**13** with *m*-CPBA in $CH_2Cl_2$ gave a mixture of β-epoxide (D-**15**) and α-epoxide (D-**16**) in a 1:4 ratio. Reaction of D-**13** with NBS[21] followed by treatment with NaOMe in MeOH resulted in a similar ratio of the epoxides. Interestingly, the use of NIS[22] instead of NBS resulted in a mixture of D-**15** and D-**16** in the 1:10 ratio. The structure of D-**16** was confirmed indirectly after its conversion to bromohydrins (D-**18**, D-**19**). Treatment of D-**16** with LiBr and AcOH[23] gave a mixture of bromohydrins (D-**18**/D-**19** = 7:3). On the basis of $^1$H NMR analysis, the major bromohydrin D-**18** was found to have a structure shown in Figure 5, thus confirming the structure of D-**16** as α-epoxide. Apparently, the ring-opening reaction of the α-epoxide D-**16** did not follow the diaxial opening rule. The reason for this observation is thought to be the influence of the vicinal benzyloxy group at C3, which may hinder the attack of the bromide anion at C2 site. The specific synthesis of the β-epoxide D-**15** was accomplished from 1,2-diol D-**3d** via the orthoacetate and bromoacetoxy intermediates.[24] Ring opening of the 1,2-β-epoxide D-**15** by treatment with aq $HClO_4$[25] in acetone gave carba-α-mannose derivative D-**17** exclusively, presumably due to the stereoselective diaxial opening (The Fürst–Plattener's rule). The configurations of D-**17** are confirmed by analysis of the H1–H5 coupling constants ($J_{H1–H2} = J_{H2–H3} = 2.8$ Hz, $J_{H3–H4} = 8.8$ Hz, $J_{H4–H5} = 9.0$ Hz) in the $^1$H NMR spectrum.

### 2.3. Transformation of carba-β-D-idopyranose to carba-α-D-idopyranose, carba-β-D-gulopyranose, and carba-α-D-gulopyranose derivatives

C1 and/or C2 stereoinversion of the carba-β-idose derivative D-**4a** gave carba-β-gulose D-**21**, carba-α-idose D-**23**, and carba-α-gulose D-**25** derivatives (Scheme 3). Due to the variance of the C4 stereochemistry of carba-β-idose D-**4d** from that of carba-β-altrose, the oxidation/reduction protocol resulted in much decreased selectivities in the inversion of C1 and C2 stereochemistry. However, carba-α-idose D-**23** and carba-α-gulose D-**25** could be derived from 1,2-β-epoxide derivative D-**22** with excellent stereoselectivities.

The 1,2-diol derivative D-**4d** was prepared by protecting the 3- and 4-OH groups as benzyl ether and removal of the MOM groups in D-**4a**. Regioselective monobenzoylations of the 1,2-diol D-**4d** were carried out as follows. Treatment of D-**4d** with triethyl orthobenzoate and TSA, followed by hydrolysis in 80% aqueous AcOH,[12] gave 2-*O*-benzoates D-**4f** as the major product (D-**4e**/D-**4f** = 14:86, 85%). On the other hand, D-**4d** upon treatment with BzCl, $Et_3N$, and $Me_2SnCl_2$[26] gave 1-*O*-benzoate (D-**4e**) as the major product (D-**4e**/D-**4f** = 96:4, 98%). Oxidation of 1-*O*-benzoate (D-**4e**) with PCC gave 2-keto compound D-**20** in 97% yield. In the reduction of D-**20**, compared to that of D-**6**, the preference for equatorial alcohol was diminished presumably due to the axial 4-OBn group, which hinders the topside approach of the hydride. Treatment of D-**20** with $NaBH_4$ in $CH_2Cl_2$/MeOH (20:1) gave a mixture of carba-β-D-gulose D-**21** and D-**4e** (D-**21**/D-**4e** = 43:57). Attempts to increase the stereoselectivity by using different reducing conditions produced no improvement (D-**21**/D-**4e** = ~4:6 with $NaBH_4/CaCl_2$[27] or with $BH_3{\cdot}Me_2S$). However, the carba-β-D-gulose derivative D-**21** could be separated as pure diastereomer on silica gel. The recovered D-**4e** could be recycled for the oxidation/reduction procedure to provide more of D-**21**. The structure of carba-β-D-gulose D-**21** was confirmed by analysis of coupling constants of H1–H4, H5aα, and H5aβ ($J_{H1–H2} = 9.7$ Hz, $J_{H2–H3} = J_{H3–H4} = 3.4$ Hz, $J_{H1–H5a\alpha} = 5.0$ Hz, $J_{H1–H5a\beta} = 11.3$ Hz) in the $^1$H NMR spectrum.

Preliminary experiments on the stereoinversion of carba-β-idose D-**4f** to carba-α-idose by the oxidation/reduction protocol resulted in poor stereoselectivities regardless of the conditions examined (carba-α-idose/carba-β-idose = 1:2 by $NaBH_4$ with or without $CeCl_3$ or $CaCl_2$, for example). Although the two epimers are easily separable by column chromatography, the observed selectivity was not satisfactory from a practical viewpoint. Thus, we turned to the ring-opening reaction of β-1,2-epoxide derivative D-**22**, which fortunately gave carba-α-idose derivative D-**23** with an excellent stereoselectivity. The β-1,2-epoxide D-**22** was prepared from 1,2-diol derivative D-**4d** by sequential treatments[24] with (1) trimethyl orthoacetate, PPTS, (2) AcBr, $Et_3N$ (0.1 equiv), in $CH_2Cl_2$, and (3) NaOMe in MeOH. Ring-opening reaction of β-1,2-epoxide D-**22** with allyl alcohol[28] and TSA (0.26 equiv) gave carba-α-idose derivative D-**23** in 73% yield. In this ring-opening reaction, the nucleophile attacked only C1 of the β-1,2-epoxide D-**22** to give one stereoisomer (carba-α-idose). The structure of carba-α-idose D-**23** was confirmed by $^1$H NMR analysis ($J_{H1–H2} = J_{H2–H3} = 8.7$ Hz, $J_{H1–H5a\alpha} = 11.2$ Hz, $J_{H1–H5a\beta} = 4.7$ Hz) in acetone-$d_6$ as an inverted chair conformer in which C1–C4 substituents have all




**Scheme 3.** Reagents and conditions: (a) NaOMe (0.3 equiv), MeOH, rt, 5h, 94%; (b) NaH (6 equiv), BnBr (6 equiv), $Bu_4NI$ (0.2 equiv), THF, rt, 78%; (c) TMSBr (15 equiv), molecular sieves 4 Å, $CH_2Cl_2$, −20 °C, 69%; (d) $Et_3N$ (2.0 equiv), $Me_2SnCl_2$ (5.4 mol %), BzCl (1.2 equiv), 0 °C, 98% (D-**4e**/D-**4f** = 94:6); (e) (i) $(EtO)_3CPh$ (2 equiv), TSA (0.03 equiv), $CH_2Cl_2$, rt, (ii) 80% AcOH, 85% (D-**4e**/D-**4f** = 14:86); (f) PCC (3.0 equiv), molecular sieves 4 Å, $CH_2Cl_2$, rt, 97% D-**20**, 99% D-**24**; (g) $NaBH_4$ (5.0 equiv), MeOH (50 equiv), $CH_2Cl_2$, −20 °C, 89% (D-**21**/D-**4e** = 43:57); (h) (i) $(CH_3O)_3CCH_3$ (1.5 equiv), PPTS (cat.), $CH_2Cl_2$, (ii) AcBr (3.0 equiv), $Et_3N$ (0.1 equiv), $CH_2Cl_2$, (iii) NaOMe/MeOH, 95%; (i) TSA (0.26 equiv), allyl alcohol, rt, 3.5 h, 73%; (j) L-Selectride™ (5 equiv), THF, −20 °C, 20 min, 73%.

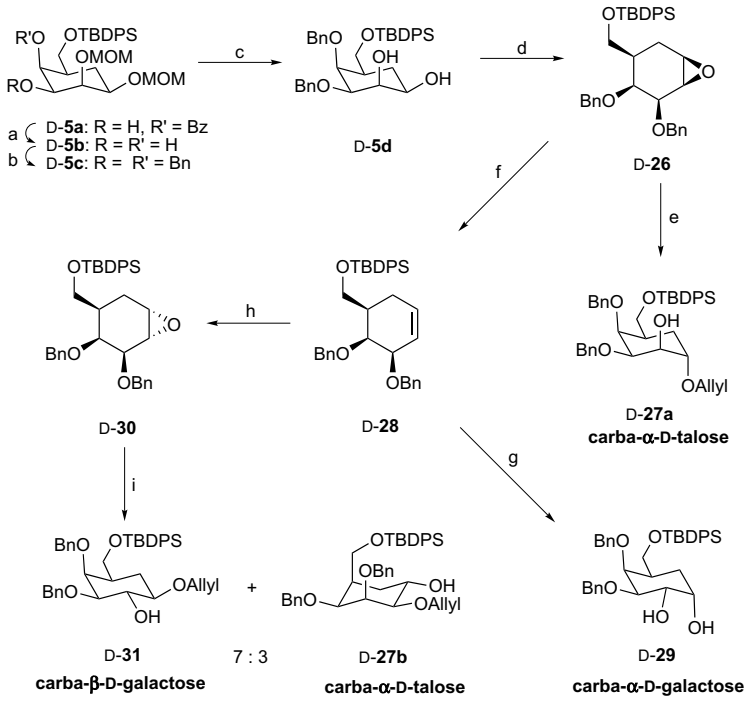
equatorial orientations, while the C5-TBDPSO$CH_2$ group occupies the axial position. Oxidation of carba-α-idose derivative D-**23** with PCC gave the 2-keto derivative D-**24**, which upon reduction with L-Selectride™[29] gave exclusively the desired carba-α-gulose derivative D-**25** (73%) without formation of D-**23**. The structure of D-**25** was again confirmed by $^1H$ NMR analysis ($J_{H1–H2} = 3.4$ Hz, $J_{H2–H3} = 3.5$ Hz, $J_{H3–H4} = 3.7$ Hz, $J_{H1–H5a\alpha} = 3.4$ Hz, $J_{H1–H5a\beta} = 3.4$ Hz) in benzene-$d_6$ with the conformation as shown in Scheme 3.

### 2.4. Transformation of carba-β-D-talopyranose to carba-α-D-talopyranose, carba-β-D-galactopyranose, and carba-α-D-galactopyranose derivatives

Regio- and stereoselective modifications of the C1 and/or C2 stereochemistry in carba-β-D-talose derivative D-**5** gave carba-α-D-talose D-**27a**, carba-α-D-galactose D-**29**, and carba-β-D-galactose D-**31** derivatives (Scheme 4). Due to the same stereochemistry at C3 of D-**5d** as that of carba-β-mannose derivative D-**3d**, an analogous strategy employing epoxidation/ring-opening and olefination/dihydroxylation was successfully applied to the carba-β-talose derivative. Inversion of the C2 stereochemistry was carried out via a ring-opening reaction of the 1,2-α-epoxide derivative rather than Mitsunobu reaction.

The 1,2-diol derivative D-**5d** was prepared by the usual protection and deprotection of D-**5a**. Stereoselective preparation of the 1,2-β-epoxide derivative D-**26** was carried out from the 1,2-diol derivative D-**5d** by the same procedure as used for the synthesis of other 1,2-β-epoxide derivatives, D-**15** and D-**22**. Ring-opening reaction of the 1,2-β-epoxide D-**26** by treatment with allyl alcohol and TSA (0.4 equiv) gave carba-α-D-talose derivative D-**27a** in 68% yield. In the ring opening, allyl alcohol again attacked only the C1 position of the 1,2-β-epoxide to give one stereoisomer, carba-α-D-talose. Although there are three axial substituents (C1, C2, and C4) in the cyclohexane ring, the carba-α-D-talose derivative D-**27a** was found to have a conventional chair conformation as shown in Scheme 4 on the basis of the $^1H$ NMR analysis in $CDCl_3$ ($J_{H2–H3} = 2.3$ Hz, $J_{H3–H4} = 2.3$ Hz, $J_{H4–H5} =$ small, $J_{H1–H5a\alpha} = 2.7$ Hz, $J_{H1–H5a\beta} = 2.3$ Hz for D-**27a**).

An initial attempt to synthesize 1,2-olefin derivative D-**28** by didehydroxylation of 1,2-diol derivative D-**5d** was not successful, as the treatment of D-**5d** with $PPh_3$, imidazole, and $I_2$ resulted in a low yield (<30%)




**Scheme 4.** Reagents and conditions: (a) NaOMe (0.3 equiv), MeOH, rt, 4.5 h, 95%; (b) NaH (6 equiv), BnBr (6 equiv), $Bu_4NI$ (0.2 equiv), THF, rt, 94%; (c) TMSBr (20 equiv), molecular sieves 4 Å, $CH_2Cl_2$, −20 °C, 91%; (d) (i) $(CH_3O)_3CCH_3$ (3.2 equiv), PPTS, $CH_2Cl_2$, (ii) AcBr (3.0 equiv), $Et_3N$ (0.1 equiv), $CH_2Cl_2$, (iii) NaOMe (3 equiv)/MeOH, 99%; (e) TSA (0.4 equiv), allyl alcohol, rt, 26 h, 68%; (f) (i) $PPh_3$ (2 equiv), $I_2$ (2 equiv), DMF, rt, (ii) Zn powder (5 equiv), rt, 92%; (g) $OsO_4$ (cat.), NMO (2 equiv), acetone/water (8:1), 6 h, rt, 91%; (h) *m*-CPBA, $CH_2Cl_2$, 22 h, rt, D-**30**/D-**26** = 54%:42%; (i) TSA (0.26 equiv), allyl alcohol, 40 °C, 10 h, 53.8% D-**31**, 23% D-**27b**.

of D-**28** with a number of by-products. Since the same conditions for the didehydroxylation were successfully applied to the carba-β-mannose derivative D-**3d**, the failure of the reaction with D-**5d** must be related to the opposite stereochemistry at C4 in D-**5d**. The –OBn group with axial orientation at C4 may sterically hinder the formation of the phosphonium ion intermediate, which is assumed to be involved in this reaction. Thermolysis of the 1,2-orthoformate derivative,[30] prepared from 1,2-diol D-**5d**, was tried in $Ac_2O$ only to result in decomposition of the starting material. However, it was found that treatment of 1,2-β-epoxide D-**26** with $PPh_3$ (2 equiv) and $I_2$ (2 equiv) in DMF,[31] followed by addition of Zn powder (5 equiv), gave the desired 1,2-olefin derivative, D-**28**, in 92% yield. Dihydroxylation of the 1,2-olefin derivative D-**28** with a catalytic amount of $OsO_4$ and an excess of NMO (2 equiv) gave a carba-α-galactose derivative D-**29** as the sole product in 91% yield. The structure and conformation of D-**29** was confirmed by $^1$H NMR analysis as shown in Scheme 4 ($J_{H1–H2} = 3.2$ Hz, $J_{H2–H3} = 9.7$ Hz, $J_{H3–H4} = 2.2$ Hz, $J_{H4–H5} = 2.2$ Hz, $J_{H1–H5a\alpha} = 3.0$ Hz, $J_{H1–H5a\beta} = 3.0$ Hz).

Epoxidation of D-**28** with *m*-CPBA gave a mixture of 1,2-α-epoxide D-**30** (54%) and 1,2-β-epoxide D-**26** (42%). Compared to the epoxidation of D-**13**, treatment of D-**28** with *m*-CPBA was expected to give more α-epoxide because the axial benzyloxy group at C4 might provide additional steric hindrance to the topside approach of peroxide. The observed stereoselectivity suggests that the course of the epoxidation with *m*-CPBA is influenced not only by steric hindrance but also by some other factors, such as hydrogen bonding or hydrophobic interactions. Ring-opening reaction of the 1,2-α-epoxide D-**30** was effected with allyl alcohol and TSA (0.26 equiv) at 40 °C to afford the remaining stereoisomer, a carba-β-D-galactose derivative D-**31** together with a minor amount of a carba-α-D-talose derivative D-**27b**. The carba-β-galactose derivative D-**31** was obtained by an apparent diequatorial ring-opening process; a similar stereoselectivity was previously seen in the ring-opening reaction of D-**16** with LiBr and AcOH. The structures and conformations of the carba-β-D-galactose D-**31** derivatives were confirmed as shown in Scheme 4 by $^1$H NMR analysis ($J_{H1–H2} = 9.4$ Hz, $J_{H2–H3} = 9.7$ Hz, $J_{H3–H4} = 2.1$ Hz, $J_{H4–H5} = 2.1$ Hz, $J_{H1–H5a\beta} = 11.6$ Hz).

In summary, we have successfully synthesized all 16 carbasugar stereoisomers by the systematic manipulation of the C1–C4 stereochemistry of one readily prepared stereoisomer, that is, a carba-β-altrose derivative.

## 3. Conclusion

We have successfully developed divergent synthetic routes to all possible carbahexopyranose stereoisomers and their 1,2-epoxide derivatives by systematically adjusting the hydroxyl stereochemistry of a carba-β-altropyranose derivative, which is readily prepared as both D- and L-form from commercially available 3-cyclohexene-1-carboxylic acid. The carbasugar building blocks that are made available by these synthetic routes should find use in the synthesis of various oligosaccha-

ride mimetics. In fact, we are currently carrying out the combinatorial preparation of analogues of KRN7000, an extremely exciting molecule displaying anticancer and immunomodulatory activity, by attaching these carbasugar residues to the readily available ceramide library of sphingosine and phytosphingosine.[32] Furthermore, it is now expected that the role of carbohydrates in the life processes may be studied more efficiently with the availability of these carbohydrate mimetics. Eventually, the 'glyco-mimetics' based on these synthetic carbasugars are hoped to provide valuable therapeutic tools for carbohydrate-related diseases, such as diabetics, cancers, and viral diseases.

## 4. Experimental

### 4.1. General procedure

All non-hydrolytic reactions were carried out in oven-dried glassware under an inert atmosphere of dry argon or nitrogen. All commercial chemicals were used as obtained without further purification, except for solvents, which were purified and dried by standard methods prior to use. Melting points were determined on a Thomas–Hoover apparatus and are uncorrected. Analytical TLC was performed on Merck 60 F254 silica gel plates (0.25 mm thickness) and visualization done with UV light, and/or by spraying a 5% solution of phosphomolybdic acid followed by charring with a heat gun. Column chromatography was performed on Merck 60 silica gel (70–230 mesh or 230–400 mesh). NMR spectra were recorded on a Bruker AM 300 or DPX 300 spectrometer. Tetramethylsilane was used as the internal standard for $^1$H NMR. Low resolution mass spectra were determined on a micromass PLATFORM II (EI, FAB) and high resolution mass spectra (FAB) on a JMS-700 at the Korea Basic Science Center, Daegu, Korea. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. The standard extractive work-up procedure consisted of pouring into a large amount of water, extracting with organic solvent indicated, washing the combined extracts successively with water and brine, drying the extract on anhydrous $Na_2SO_4$ or $MgSO_4$, and evaporating the solvent.

### 4.2. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-altropyranose, D-2b

To a solution of D-**2a** (515 mg, 1.02 mmol) in dry THF (20 ml) at 0 °C was added NaH (267 mg, 55% in paraffin liquid, 6.12 mmol). After stirring for 30 min at rt, BnBr (0.727 ml, 6.12 mmol) and $Bu_4NI$ (75.6 mg, 0.204 mmol) were added. After stirring for 48 h at rt, the reaction mixture was quenched with drops of satd aq $NaHCO_3$ and worked up by a standard extractive procedure with EtOAc. A chromatography on silica gel gave compound D-**2b** (633 mg, 90.2%) as a colorless oil. D-**2b**: $[\alpha]_D^{25} = -18.1$ (*c* 1.76, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (s, 9H, –C(C$H_3$)$_3$), 1.88 (dt, $J = 12.2$, 4.0 Hz, 1H, H-5a$_{eq}$), 2.03 (app q, $J = 12.0$ Hz, 1H, H-5a$_{ax}$), 2.20 (m, 1H, H-5), 3.37 (s, 3H, OCH$_2$OC$H_3$), 3.41 (s, 3H, OCH$_2$OC$H_3$), 3.75 (dd, $J = 9.7$, 2.4 Hz, 1H, H-6$_\alpha$), 3.90 (dd, $J = 10.6$, 2.6 Hz, 1H, H-4), 3.96–4.1 (m, 4H, H1, H2, H-3, H-6$_\beta$), 4.44–4.80 (m, 8H, 2× –OC$H_2$Ph and 2× –OC$H_2$OCH$_3$), 7.2–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.1, 27.6, 29.02, 38.7, 56.0, 56.3, 65.0, 72.5, 73.8, 74.1, 76.4, 77.1, 77.2, 96.0, 98.2, 128.1, 128.3, 128.4, 128.5, 128.9, 129.0, 130.1, 130.2, 134.5, 134.7, 136.4, 136.5, 139.4; MS (FAB) *m*/*z* 707 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{41}H_{52}O_7SiNa$ 707.3380 found 707.3381 ($M^+$+Na).

### 4.3. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-altropyranose, D-2c

To a solution of D-**2b** (304 mg, 0.443 mmol) and molecular sieves 4 Å (400 mg, powder) in dry $CH_2Cl_2$ (10 ml) at −20 °C was added TMSBr (0.64 ml, 4.7 mmol). After stirring for 40 min at −20 °C, the reaction mixture was poured into satd aq $NaHCO_3$ (30 ml). After filtering the resulting mixture on Celite, the filtrate was extractively worked up with EtOAc. The crude product was chromatographed on silica gel to give compound D-**2c** (170 mg, 64%) as a colorless oil. D-**2c**: $[\alpha]_D^{15} = +2.6$ (*c* 1.51, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.08 (s, 9H, –C(C$H_3$)$_3$), 1.75–1.9 (m, 2H, H-5a$_{ax}$ and H-5a$_{eq}$), 1.93 (d, $J = 3.8$ Hz, 1H, OH), 2.25 (m, 1H, H-5), 2.32 (d, $J = 1.8$ Hz, 1H, –OH), 3.75 (dd, $J = 10.0$, 4.8 Hz, 1H, H-6$_\alpha$), 3.87 (dd, $J = 10.0$, 4.9 Hz, 1H, H-6$_\beta$), 3.93 (dd, $J = 5.5$, 2.6 Hz, 1H, H-3), 3.99 (dd, $J = 8.6$, 2.6 Hz, 1H, H4), 4.05–4.16 (m, 2H, H-1 and H-2), 4.47–4.7 (m, 4H, 2× –OC$H_2$Ph), 7.2–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 30.2, 38.9, 65.4, 69.1, 71.9, 72.5, 73.3, 76.4, 77.0, 128.1, 128.3, 128.9, 129.0, 130.2 (2s), 134.4 (2s), 136.3, 136.4, 139.3, 139.4; MS (FAB) *m*/*z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2863 ($M^+$+Na).

### 4.4. 1-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-altropyranose, D-2d and 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-altropyranose, D-2e

To a solution of D-**2c** (100 mg, 0.167 mmol) in $CH_2Cl_2$ (2 ml) at rt were added $(EtO)_3CPh$ (76 μl, 0.335 mmol) and TSA (3.2 mg, 0.0167 mmol) in portions. After stirring for 30 min, the reaction mixture was concentrated by evaporation and the resulting residue treated with 80% aq AcOH (0.5 ml) and stirred for 10 min at rt. A standard extractive work-up with EtOAc, followed by chromatography on silica gel, gave compounds D-**2d** (46.5 mg, 39.6%) and D-**2e** (61.6 mg, 52.5%) as colorless oils. D-**2d**: $[\alpha]_D^{16} = +10.25$ (*c* 1.77, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.08 (s, 9H, –C(C$H_3$)$_3$), 1.97 (dt, $J = 12.7$, 4.3 Hz, 1H, H-5a$_{eq}$), 2.11 (app q, $J = 12.2$ Hz, 1H, H-5a$_{ax}$), 2.35 (m, 1H, H-5), 3.75 (dd, $J = 9.9$, 3.6 Hz, 1H, H-6$_\alpha$), 3.94 (dd, $J = 9.9$, 4.4 Hz, 1H, H-6$_\beta$), 4.03–4.05 (m, 2H, H-1, H-3, H-4), 4.35 (t, $J = 3.6$ Hz, 1H, H-2), 4.46–4.75 (m, 4H, 2× –OC$H_2$Ph), 5.49 (ddd, $J = 10.6$, 4.7, 3.0 Hz, 1H, H-1), 7.2–8.1 (m, 25H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.5, 26.7, 27.1, 38.0, 64.3, 69.8, 71.9, 72.7, 72.8, 75.5, 75.6, 127.6, 127.8, 127.9, 128.5, 128.6, 129.7, 129.8, 130.4, 133.3, 133.7, 135.8, 135.9, 138.5, 138.7, 165.8; MS (FAB) *m*/*z* 723 ($M^+$+Na); MS

(FAB) *m*/*z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3112 ($M^+$+Na); D-**2e**: $[\alpha]_D^{16} = -17.8$ (*c* 1.80, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.12 (s, 9H, –C($CH_3$)$_3$), 1.92 (m, 1H, H-5$a_{eq}$), 2.14 (app q, $J = 12.0$ Hz, 1H, H-5$a_{ax}$), 2.25 (m, 1H, H-5), 3.67 (dd, $J = 9.8$, 1.6 Hz, 1H, H-6$_\alpha$), 3.95 (dd, $J = 10.4$, 2.6 Hz, 1H, H-4), 4.06–4.11 (m, 2H, H-3, H-6$_\beta$), 4.33 (m, 1H, H-1), 4.38–4.78 (m, 4H, 2× –OC$H_2$Ph), 5.56 (app t, 1H, H-2), 7.12–8.1 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.6, 27.1, 31.3, 37.6, 63.7, 67.3, 72.0, 73.2, 73.4, 74.1, 75.9, 127.6, 127.8, 127.9, 128.0, 128.4, 128.5, 128.7, 129.8, 129.9, 130.0, 133.4, 133.6, 135.8, 135.9, 138.3, 138.4, 167.2; MS (FAB) *m*/*z* 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3112 ($M^+$+Na).

### 4.5. (2*R*,4*S*,5*R*,6*R*)-2-Benzoyloxy-4-(*tert*-butyl-diphenyl-silanyloxymethyl)-5,6-di-benzyloxy-cyclohexanone, D-6

To a stirred mixture of D-**2d** (30 mg, 42.8 μmol) and molecular sieves 4 Å (powder, 30 mg) in $CH_2Cl_2$ (2 ml) at rt was added PCC (27.6 mg, 0.128 mmol). After stirring for 5 h, the reaction mixture was filtered through a silica gel column and washed with EtOAc/*n*-hexane (1:4). The filtrate was concentrated to give D-**6** (29.8 mg, 42.6 μmol, 99.6%) as colorless oil. D-**6**: $[\alpha]_D^{20} = +51.65$ (*c* 1.49, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C($CH_3$)$_3$), 1.95 (app q, $J = 12.9$ Hz, 1H, H-3$a_{ax}$), 2.36 (ddd, $J = 12.6$, 6.9, 4.1 Hz, 1H, H-3$a_{eq}$), 2.72 (m, 1H, H-4), 3.68 (dd, $J = 10.7$, 2.7 Hz, 1H, H-5), 3.82 (dd, $J = 10.0$, 2.2 Hz, 1H, H-7$_\alpha$), 4.06 (dd, $J = 10.0$, 4.3 Hz, 1H, H-7$_\beta$), 4.30 (d, $J = 2.6$ Hz, 1H, H-6), 4.33–4.92 (m, 4H, 2× –OC$H_2$Ph), 6.04 (dd, $J = 13.0$, 6.9 Hz, 1H, H-2), 7.2–8.2 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 30.8, 38.4, 63.8, 72.1, 72.6, 75.2, 79.8, 81.4, 128.3, 128.4, 128.8, 129.0, 129.1, 129.2, 129.5, 130.3, 130.4, 130.5, 130.6, 134.0, 136.3, 136.4, 137.5, 138.4, 166.3 (Ph*C*=O), 204.8 (C-1); MS (FAB) *m*/*z* 699 ($M^+$+H), 721 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{46}O_6SiNa$ 721.2961 found 721.2967 ($M^+$+Na).

### 4.6. 1-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldi-phenyl)silyl-5a-carba-β-D-allopyranose, D-7

To a solution of D-**6** (15 mg, 21.4 μmol) in THF (1.8 ml) at 0 °C, $BH_3{\cdot}Me_2S$ (107 μmol, 53.5 μl of 2 M solution in THF) was added. After stirring for 1 h at rt, the reaction mixture was quenched with a few drops of MeOH and concentrated. The residue was filtered on silica gel and the filtrate was concentrated to give a mixture of D-**7** and D-**2d** (85:5). This mixture was treated with PCC (13.8 mg, 3.0 equiv) in $CH_2Cl_2$ (1.5 ml) for 2 h at rt and the resulting mixture was filtered on silica gel. The filtrate was concentrated and chromatographed to give D-**6** (4.5 mg, 30%) and a mixture of D-**7**/D-**2d** (95:5 by $^1H$ NMR analysis, 9 mg, 60%) as colorless oils. D-**7**: $[\alpha]_D^{22} = -6.0$ (*c* 0.45, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.10 (s, 9H, –C($CH_3$)$_3$), 1.67 (app q, $J = 12.5$ Hz, 1H, H-5$a_{ax}$), 2.09 (dt, $J = 13.0$, 4.6 Hz, 1H, H-5$a_{eq}$), 2.40 (m, 1H, H-5), 2.50 (br d, $J = 10.1$ Hz, 1H, –OH), 3.60–3.70 (m, 2H, H-2, H-6$_\alpha$), 3.73 (dd, $J = 9.8$, 2.6 Hz, 1H, H-4), 4.02 (dd, $J = 9.9$, 4.0 Hz, 1H, H-6$_\beta$), 4.26 (pseudo t, 1H, H-3), 4.5–5.1 (m, 4H, 2× –OC$H_2$Ph), 5.31 (ddd, $J = 11.3$, 9.7, 5.1 Hz, 1H, H-1), 7.2–8.1 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 30.2, 38.6, 64.2, 72.8, 74.4, 74.9, 75.3, 78.5, 79.8, 128.2, 128.3, 128.4, 129.0, 129.1, 130.3, 130.35, 130.41, 131.2, 133.6, 134.1, 134.2, 136.31, 136.36, 138.8, 139.3, 167.4 (Ph*C*=O); MS (FAB) *m*/*z* 701 ($M^+$+H), 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3112 ($M^+$+Na).

### 4.7. (2*S*,3*R*,4*R*,5*S*)-2-Benzoyloxy-5-(*tert*-butyl-diphenyl-silanyloxymethyl)-3,4-di-benzyloxy-cyclohexanone, D-8

To a stirred mixture of D-**2e** (40 mg, 57.1 μmol) and molecular sieves 4 Å (powder, 40 mg) in $CH_2Cl_2$ (1.5 ml) at rt was added PCC (37 mg, 171.2 μmol). After refluxing for 4 h, the reaction mixture was filtered through a silica gel column and washed with EtOAc/*n*-hexane (1:4). The filtrate was concentrated to give D-**8** (37.4 mg, 53.5 μmol, 93.7%) as a colorless oil. D-**8**: $[\alpha]_D^{18} = -26.5$ (*c* 1.87, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.04 (s, 9H, –C($CH_3$)$_3$), 2.42 (app d, $J = 14.7$ Hz, 1H, H-6$_{eq}$), 2.50 (m, 1H, H-5), 2.36 (dd, $J = 14.5$, 6.8 Hz, 1H, H-6$_{ax}$), 3.47 (dd, $J = 10.7$, 6.8 Hz, 1H, H-7$_\alpha$), 3.61 (dd, $J = 10.8$, 4.1 Hz, 1H, H-7$_\beta$), 4.25 (pseudo t, $J = 3.3$ Hz, 1H, H-4), 4.29 (dd, $J = 9.8$, 2.6 Hz, 1H, H-3), 4.6–4.9 (m, 4H, 2× –OC$H_2$Ph), 5.96 (d, $J = 9.7$ Hz, 1H, H-2), 7.2–8.2 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.9, 27.6, 38.7, 40.4, 65.1, 73.4, 73.7, 76.6, 79.0, 79.3, 128.39, 128.44, 128.5, 129.0, 129.1, 130.5, 130.6, 130.7, 133.3, 133.5, 133.8, 136.3, 136.4, 138.7, 139.0, 166.2 (Ph*C*=O), 202.3 (C-1); MS (FAB) *m*/*z* 699 ($M^+$+H), 721 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{46}O_6$-SiNa 721.2961 found 721.2960 ($M^+$+Na).

### 4.8. 2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldi-phenyl)silyl-5a-carba-α-D-altropyranose, D-9a

To a solution of D-**8** (43 mg, 61.5 μmol) in $CH_2Cl_2$/MeOH (20:1, 5 ml) at −10 °C was added $NaBH_4$ (11.63 mg, 0.307 mmol) over 20 min. After stirring for 90 min at −10 °C, the reaction mixture was treated with AcOH (three drops) and stirred for an additional 1 h. The reaction mixture was filtered on a silica gel pad and the filtrate was concentrated to give a mixture (D-**9a**/D-**2e** = 3:1 by $^1H$ NMR analysis). This mixture was chromatographed to give a mixture of D-**9a** (29.6 mg, 68.6%) and D-**2e** (8 mg, 18.5%). D-**9a**: $[\alpha]_D^{19} = -13.7$ (*c* 1.48, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.14 (s, 9H, –C($CH_3$)$_3$), 1.96 (d, $J = 12.8$ Hz, 1H, H-5$a_{eq}$), 2.30 (td, $J = 13.5$, 2.9 Hz, 1H, H-5$a_{ax}$), 2.44 (m, 1H, H-5), 3.66 (dd, $J = 9.9$, 2.2 Hz, 1H, H-6$_\alpha$), 3.76 (br d, $J = 10.1$ Hz, 1H, –OH), 4.0–4.1 (m, 2H, H-1, and H-6$_\beta$), 4.13 (pseudo t, $J = 2.9$ Hz, 1H, H-3), 4.21 (dd, $J = 9.9$, 2.9 Hz, 1H, H-4), 4.4–4.85 (m, 4H, 2× –OC$H_2$Ph), 5.54 (pseudo t, $J = 3.2$ Hz, 1H, H-2), 7.1–8.2 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 20.1, 27.7, 32.4, 35.1, 64.3, 69.2, 72.1, 72.6, 74.3, 76.3, 76.6, 128.3, 128.40, 128.43, 128.7, 128.8, 129.0, 129.18, 129.22, 130.3, 130.4, 134.0, 134.2, 136.3, 136.4, 138.1, 138.9, 165.8 (Ph*C*=O); MS (FAB) *m*/*z* 701 ($M^+$+H), 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3112 ($M^+$+Na).

### 4.9. 2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-di-phenyl)silyl-1-*O*-methoxymethyl-5a-carba-α-D-altropyranose, D-9b

To a solution of D-**9a** (25 mg, 35.8 μmol) in $CH_2Cl_2$ (3 ml) at 0 °C were added $(i\text{-Pr})_2NEt$ (81 μl, 0.465 mmol) and MOM–Cl (35.3 μl, 0.465 mmol), and the resulting mixture was refluxed for 15 h. After cooling to rt, the reaction mixture was diluted with $CH_2Cl_2$ and washed with satd aq $NaHCO_3$, 1 M HCl, and satd aq $NaHCO_3$. The organic layer was dried over $MgSO_4$, concentrated, and chromatographed to give D-**9b** (22.4 mg, 30.1 μmol, 84.0%) as a colorless oil. D-**9b**: $[\alpha]_D^{21} = -2.8$ (*c* 1.12, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.10 (s, 9H, $-C(CH_3)_3$), 1.90–2.15 (m, 2H, H-5$a_{eq}$ and H-5$a_{ax}$), 2.38 (m, 1H, H-5), 3.25 (s, 3H, $-OCH_2OCH_3$), 3.62 (dd, $J = 10.3$, 6.6 Hz, 1H, H-6$_\alpha$), 3.75–3.82 (m, 2H, H-3, H-6$_\beta$), 3.94 (m, 1H, H-1), 4.06 (dd, $J = 4.9$, 2.7 Hz, 1H, H-4), 4.5–4.75 (m, 6H, 2 × $-OCH_2Ph$ and $-OCH_2OCH_3$), 5.73 (t, $J = 7.8$ Hz, 1H, H-2), 7.1–8.2 (m, 25H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.9, 27.6, 29.3, 38.6, 56.0, 65.2, 72.6, 72.7, 74.8, 74.9, 75.9, 77.6, 96.2, 128.03, 128.06, 128.4, 128.5, 128.8, 128.9, 129.0, 130.4, 130.5, 131.2, 133.5, 133.98, 134.01, 136.3, 139.0, 139.5, 166.2 (Ph*C*=O); MS (FAB) *m*/*z* 745 ($M^+$+H), 767 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{46}H_{52}O_7SiNa$ 767.3380 found 767.3380 ($M^+$+Na).

### 4.10. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1-*O*-methoxymethyl-5a-carba-α-D-altropyranose, D-9c

To a solution of D-**9b** (20 mg, 26.8 μmol) in MeOH (2 ml) was added NaOMe (134 μmol, 30.7 μl of 25% solution in MeOH). After stirring for 14 h at rt, the reaction mixture was treated with AcOH (150 μmol, 8.75 μl) and concentrated. The residue was dissolved in $CH_2Cl_2$, filtered on silica gel, and washed with EtOAc/*n*-hexane (1:2). The filtrate was concentrated to give D-**9c** (16.1 mg, 93.6%) as a colorless oil. D-**9c**: $[\alpha]_D^{18} = -8.6$ (*c* 0.80, $CHCl_3$); $^1H$ NMR ($C_6D_6$) $\delta$ 1.22 (s, 9H, $-C(CH_3)_3$), 1.99 (br dd, $J = 12.5$, 4.4 Hz, 1H, H-5$a_{eq}$), 2.25 (app td, $J = 12.5$, 5.8 Hz, 1H, H-5$a_{ax}$), 2.42 (m, 1H, H-5), 3.21 (s, 3H, $OCH_2OCH_3$), 3.24 (br s, 1H, –OH), 3.58 (dd, $J = 9.3$, 2.6 Hz, 1H, H-3), 3.6–3.8 (m, 3H, H-1, H-6$_\alpha$, and H-6$_\beta$), 4.04 (pseudo t, $J = 2.6$ Hz, 1H, H-4), 4.47 (t, $J = 9.3$ Hz, 1H, H-2), 4.6–4.8 (m, 6H, 2 × $-OCH_2Ph$ and $-OCH_2OCH_3$), 6.9–7.9 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.0, 27.6, 28.4, 30.4, 39.9, 56.1, 65.1, 72.6, 72.9, 74.4, 74.6, 79.0, 80.8, 97.3, 128.1, 128.28, 128.35, 128.4, 128.5, 128.9, 129.1, 130.5, 133.9, 134.0, 136.21, 136.24, 139.1, 139.6; MS (FAB) *m*/*z* 663 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{39}H_{48}O_6SiNa$ 663.3118 found 663.3118 ($M^+$+Na).

### 4.11. (2*R*,3*S*,4*S*,6*R*)-2,3-Di-benzyloxy-4-(*tert*-butyl-diphenyl-silanyloxymethyl)-6-methoxymethyloxy-cyclohexanone, D-10

To a stirred mixture of D-**9c** (14 mg, 21.8 μmol) and molecular sieves 4 Å (powder, 20 mg) in $CH_2Cl_2$ (1.5 ml) at rt was added PCC (14.1 mg, 65.5 μmol). After refluxing for 11 h, the reaction mixture was filtered through a silica gel column and washed with EtOAc/*n*-hexane (1:2). The filtrate was concentrated to give D-**10** (12.4 mg, 89.0%) as colorless oil. D-**10**: $[\alpha]_D^{20} = +3.0$ (*c* 0.62, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.03 (s, 9H, $-C(CH_3)_3$), 2.10 (app dd, $J = 12.7$, 6.8 Hz, 1H, H-5$_{eq}$), 2.26 (dt, $J = 12.3$, 6.0 Hz, 1H, H-5$_{ax}$), 2.36 (m, 1H, H-4), 3.39 (s, 3H, $-OCH_2OCH_3$), 3.72 (app d, $J = 6.54$ Hz, 2H, H-7$_\alpha$ and H-7$_\beta$), 4.25–4.37 (m, 3H, H-2, H-3, and H-6), 4.4–4.9 (m, 6H, 2 × $-OCH_2Ph$ and $-OCH_2OCH_3$), 7.2–7.7 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.8, 27.5, 32.3, 40.1, 56.4, 65.5, 72.9, 73.4, 76.9, 81.6, 82.6, 96.4, 128.07, 128.13, 128.4, 128.6, 128.9, 129.1, 130.6, 133.5, 133.6, 136.20, 136.22, 138.6, 139.3, 204.7 (C-1); MS (FAB) *m*/*z* 661 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{39}H_{46}O_6SiNa$ 661.2961 found 661.2965 ($M^+$+Na).

### 4.12. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1-*O*-methoxymethyl-5a-carba-α-D-allopyranose, D-11

To a solution of D-**10** (10 mg, 15.6 μmol) in $CH_2Cl_2$/MeOH (0.6 ml) at −10 °C was added $NaBH_4$ (3.0 mg, 78.3 mmol). After stirring for 30 min at −10 °C, the reaction mixture was treated with AcOH (two drops) and stirred for an additional 1 h. The reaction mixture was filtered on silica gel pad and the filtrate was concentrated to give a residue (D-**11**/D-**9c** = >99:1 by $^1H$ NMR analysis). This mixture was chromatographed to give D-**11** (10.0 mg, quantitative). D-**11**: $[\alpha]_D^{22} = +16.7$ (*c* 0.50, $CHCl_3$); $^1H$ NMR ($C_6D_6$ with $D_2O$ one drop) $\delta$ 1.23 (s, 9H, $-C(CH_3)_3$), 1.57 (ddd, $J = 14.2$, 10.4, 3.2 Hz, 1H, H-5$a_{ax}$), 2.26 (dt, $J = 14.3$, 4.7 Hz, 1H, H-5$a_{eq}$), 2.68 (m, 1H, H-5), 3.23 (s, 3H, $OCH_2OCH_3$), 3.47 (dd, $J = 9.1$, 2.2 Hz, 1H, H-4), 3.64 (br s, 1H, H-2), 3.78 (m, 1H, H-1), 3.80 (dd, $J = 9.7$, 3.6 Hz, 1H, H-6$_\alpha$), 3.98 (br s, 1H, H-3), 4.0 (dd, $J = 9.8$, 5.3 Hz, H-6$_\beta$), 4.36–4.93 (m, 6H, 2 × $-OCH_2Ph$ and $-OCH_2OCH_3$), 7.1–7.8 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.9, 27.6, 30.4, 37.4, 56.2, 64.9, 71.3, 73.2 (2s), 76.0, 77.9, 79.3, 96.7, 128.0, 128.1, 128.25, 128.28, 128.4, 128.9, 129.0, 130.38, 130.40, 134.1, 136.2, 136.3, 138.9, 139.6; MS (FAB) *m*/*z* 663 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{39}H_{48}O_6SiNa$ 663.3118 found 663.3116 ($M^+$+Na).

### 4.13. 6-*O*-(*tert*-Butyldiphenyl)silyl-1,2-di-*O*-(methoxy-methyl)-5a-carba-β-D-mannopyranose, D-3b

To a solution of D-**3a** (912 mg, 1.45 mmol) in MeOH (10 ml) was added NaOMe (145 μmol, 33 μl of 25% solution in MeOH). After stirring for 2 h at rt, the reaction mixture was treated with AcOH (one drop) and concentrated. The residue was directly chromatographed on silica gel to give D-**3b** (671 mg, 91.7%) as a colorless oil. D-**3b**: $[\alpha]_D^{20} = -32.9$ (*c* 1.08, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.05 (s, 9H, $-C(CH_3)_3$), 1.62–1.76 (m, 3H, H-5$a_{eq}$, H-5$a_{ax}$, H-5), 3.37–3.46 (2, 6H, 2 × $OCH_2OCH_3$), 3.67–3.83 (m, 5H), 4.03 (br s, 1H), 4.65–4.85 (m, 4H, 2 × $-OCH_2OCH_3$), 7.2–7.95 (m, 10H, 2Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.9, 27.5, 28.3, 41.3, 56.2, 56.7, 66.7, 73.4, 75.2, 75.4, 82.1, 95.7, 99.2, 128.5, 130.5, 133.8, 133.9, 136.3; MS (FAB) *m*/*z* 527 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{27}H_{40}O_7SiNa$ 527.2441 found 527.2441 ($M^+$+Na).

### 4.14. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-mannopyranose, D-3c

To a solution of D-**3b** (620 mg, 1.23 mmol) in dry THF (20 ml) at 0 °C was added NaH (214 mg, 55% in paraffin liquid, 4.90 mmol). After stirring for 30 min at rt, BnBr (0.584 ml, 4.91 mmol) and $Bu_4NI$ (91 mg, 0.246 mmol) were added. After stirring for 36 h at rt, the reaction mixture was quenched with drops of satd aq $NaHCO_3$ and extractively worked up with EtOAc. A chromatography on silica gel gave compound D-**3c** (688 mg, 81.4%) as a colorless oil. D-**3c**: $[\alpha]_D^{20} = -4.5$ (*c* 1.16, $CHCl_3$); $\delta$ 1.11 (s, 9H, –C(C$H_3$)$_3$), 1.66 (m, 1H, H-5), 1.92 (dt, $J =$ 12.5, 3.7 Hz, 1H, H-5a$_{eq}$), 1.95 (app q, $J =$ 12.5 Hz, 1H, H-5a$_{ax}$), 3.44 and 3.47 (2s, 6H, 2 × –$CH_2OCH_3$), 3.46 (m, 1H, H-3), 3.64 (ddd, $J = 12.2$, 4.7, 2.3 Hz, 1H, H-1), 3.81 (dd, $J = 9.7$, 2.6 Hz, 1H, H-6$_\alpha$), 3.87 (dd, $J = 9.5$, 4.0 Hz, 1H, H-6$_\beta$), 3.88 (app t, $J = 10.0$ Hz, 1H, H-4), 4.16 (br s, 1H, H-2), 4.45–4.95 (m, 8H, 2 × –C$H_2$OCH$_3$ and 2 × –OC$H_2$Ph), 7.1–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.1, 27.6, 29.0, 42.0, 56.2 (2s), 64.6, 72.8, 73.9, 75.0, 76.0, 78.2, 84.6, 95.2, 97.7, 128.1, 128.3 (2s), 128.4, 128.5, 128.7, 129.0, 129.1, 130.3, 134.3, 134.4, 136.4 (2s), 139.2, 139.5; MS (FAB) *m*/*z* 707 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{41}H_{52}O_7SiNa$ 707.3380 found 707.3375 ($M^+$+Na).

### 4.15. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-mannopyranose, D-3d

To a solution of D-**3c** (830 mg, 1.21 mmol) and molecular sieves 4 Å (2 g, powder) in dry $CH_2Cl_2$ (8.5 ml) at −20 °C was added TMSBr (2.0 ml, 14.7 mmol). After stirring for 4 h at −20 °C, the reaction mixture was poured into satd aq $NaHCO_3$. After filtering the resulting mixture on Celite, the filtrate was extractively worked up with EtOAc. The crude product was chromatographed on silica gel to give compound D-**3d** (567 mg, 78.4%) as a colorless oil. D-**3d**: $[\alpha]_D^{20} = +2.1$ (*c* 1.00, $CHCl_3$); $^1$H NMR ($CDCl_3$, with $D_2O$ one drop) $\delta$ 1.05 (s, 9H, –C(C$H_3$)$_3$), 1.57 (m, 1H, H-5), 1.82 (dt, $J = 12.2$, 4.3 Hz, 1H, H-5a$_{eq}$), 1.95 (app q, $J = 12.3$ Hz, 1H, H-5a$_{ax}$), 3.45 (dd, $J = 9.2$, 2.8 Hz, 1H, H-3), 3.62 (ddd, $J = 11.4$, 4.7, 2.8 Hz, 1H, H-1), 3.70 (dd, $J = 9.8$, 2.5 Hz, 1H, H-6$_\alpha$), 3.77 (app t, $J = 9.5$ Hz, 1H, H-4), 3.84 (dd, $J = 9.8$, 5.0 Hz, 1H, H-6$_\beta$), 4.16 (pseudo t, $J = 2.8$ Hz, 1H, H-2), 4.4–4.9 (m, 4H, 2 × –OC$H_2$Ph), 7.0–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.1, 27.7, 31.4, 41.5, 64.3, 70.5, 71.6, 73.1, 76.0, 77.8, 84.3, 128.2, 128.4 (2s), 128.7, 129.1, 129.3, 130.4, 134.2, 134.3, 136.4, 136.5, 138.7, 139.3; MS (FAB) *m*/*z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2850 ($M^+$+Na).

### 4.16. 2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-glucopyranose, D-12

To a solution of D-**3d** (30 mg, 50.26 μmol), $PPh_3$ (79.1 mg, 301 μmol), and BzOH (36.7 mg, 301 μmol) in dry toluene (1 ml) at rt was added DEAD (52.4 mg, 301 μmol). After refluxing overnight, the reaction mixture was filtered and the filtrate concentrated and chromatographed on silica gel column to give compound D-**12** (22 mg, 62.6%) as a colorless oil. D-**12**: $[\alpha]_D^{21} = +47.9$ (*c* 0.76, $CHCl_3$); $^1$H NMR (acetone-$d_6$) $\delta$ 1.12 (s, 9H, –C(C$H_3$)$_3$), 1.78 (q, $J = 11.5$ Hz, 1H, H-5a$_{ax}$), 1.85 (m, 1H, H-5), 2.20 (m, 1H, H-5a$_{eq}$), 3.69 (app t, $J = 9.9$ (9.2) Hz, 1H, H-4), 3.75 (app t, $J = 9.3$ (9.2) Hz, 1H, H-3), 3.85 (dd, $J = 9.7$, 2.0 Hz, 1H, H-6$_\alpha$), 3.9 (m, 1H, H-1), 3.97 (dd, $J = 9.7$, 4.6 Hz, 1H, H-6$_\beta$), 4.45 (br d, $J = 5.2$ Hz, –OH), 4.57–4.92 (m, 4H, 2 × –OC$H_2$Ph), 5.25 (t, $J = 9.3$ Hz, 1H, H-2), 7.1–8.1 (m, 25H, 5Ph); $^{13}$C NMR (acetone-$d_6$) $\delta$ 20.5, 28.0, 34.8, 42.3, 65.1, 71.3, 75.9, 76.5, 80.9, 82.1, 85.7, 128.7, 129.0, 129.1, 129.3, 129.5, 129.6, 129.8, 129.9, 131.0, 131.3, 132.5, 134.3, 134.8, 134.9, 137.0, 137.1, 140.1, 140.4, 167.0 (PhC=O); MS (FAB) *m*/*z* 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3115 ($M^+$+Na).

### 4.17. (1*R*,2*R*,3*S*)-1,2-Di-benzyloxy-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-cyclohex-5-ene, D-13

To a refluxing mixture of D-**3d** (60.0 mg, 100 μmol), $PPh_3$ (105 mg, 400 μmol), and imidazole (27.2 mg, 400 μmol) in toluene (5 ml) was added a solution of $I_2$ (resublimed, 83.8 mg, 330 μmol) in toluene (1 ml). After 25 min, additional imidazole (30 mg) in toluene (1 ml) was added to the mixture. After refluxing for 3 h, the reaction mixture was cooled to rt, diluted with EtOAc (50 ml), and washed with half-saturated aqueous $Na_2S_2O_3$. An extractive work-up followed by a chromatography on silica gel gave compound D-**13** (51 mg, 90.4%) as a colorless oil. D-**13**: $[\alpha]_D^{21} = -32.5$ (*c* 1.00, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (s, 9H, –C(C$H_3$)$_3$), 2.02 (m, 1H, H-3), 2.21 (dt, $J = 18.0$, 4.9 Hz, H-4a$_{eq}$), 2.40 (m, 1H, H-4a$_{ax}$), 3.77 (m, 2H, H-2 and H-7$_\alpha$), 3.98 (dd, $J = 9.9$, 5.0 Hz, 1H, H-7$_\beta$), 4.21 (m, 1H, H-3), 4.6–4.95 (m, 4H, 2 × –OC$H_2$Ph), 5.70 (br d, $J = 10.1$ Hz, 1H, H-6, olefin), 5.81 (m, 1H, H-5, olefin), 7.1–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.6, 27.2, 28.8, 41.5, 63.7, 71.9, 74.6, 79.5, 81.8, 126.3, 127.6, 127.77, 127.83, 127.9, 128.0, 128.1, 128.5, 128.6, 128.8, 129.8, 133.8, 133.9, 135.9, 136.0, 138.9, 139.1; MS (FAB) *m*/*z* 585 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{42}O_3SiNa$ 585.2801 found 585.2808 ($M^+$+Na).

### 4.18. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-glucopyranose, D-14

To a solution of D-**13** (50 mg, 88.9 μmol) and 4-methylmorpholine-*N*-oxide (NMO) (20.9 mg, 0.178 mmol) in acetone/water (4 ml, 8:1) at rt was added a catalytic amount of $OsO_4$. After stirring for 5 h, $Na_2SO_3$ (112 mg) was added and the resulting mixture stirred for an additional 30 min at rt. The reaction mixture was diluted with EtOAc and washed with 1 M HCl and satd aq $NaHCO_3$. The organic layers were dried over $MgSO_4$, concentrated, and chromatographed on silica gel column to give compound D-**14** (53 mg, quantitative) as a colorless oil. D-**14**: $[\alpha]_D^{21} = +37.8$ (*c* 1.43, $CHCl_3$); $^1$H NMR ($CDCl_3$, with $D_2O$ one drop) $\delta$ 1.07 (s, 9H, –C(C$H_3$)$_3$), 1.68 (td, $J = 12.4$, 2.15 Hz, 1H, H-5a$_{ax}$), 1.75 (dt, $J = 14.4$, 3.7 Hz, 1H, H-5a$_{eq}$), 2.09 (m, 1H, H-5), 3.52 (dd, $J = 9.2$, 2.8 Hz,

H-2), 3.58 (t, $J = 10.0$ Hz, 1H, H-4), 3.62 (dd, $J = 9.9$, 2.1 Hz, 1H, H-6$_\alpha$), 3.73 (t, $J = 9.2$ Hz, 1H, H-3), 4.02 (dd, $J = 10.0$, 3.6 Hz, 1H, H-6$_\beta$), 4.09 (pseudo q, $J = 2.5$ Hz, 1H, H-1), 4.60–5.02 (m, 4H, 2 × –OC$H_2$Ph), 5.23 (t, $J = 9.2$ Hz, 1H, H-2), 7.1–7.63 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 31.0, 36.6, 63.6, 69.0, 75.2, 75.5, 76.1, 81.6, 84.3, 128.3, 128.38, 128.42, 128.7, 129.1, 129.5, 130.4, 134.0, 134.2, 136.39, 136.44, 139.2, 139.3; MS (FAB) *m/z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2853 ($M^+$+Na).

### 4.19. 1,2-Anhydro-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-mannopyranose, D-15 and 1,2-anhydro-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-glucopyranose, D-16

*Method A*: To a solution of D-**13** (50 mg, 88.9 μmol) in $CH_2Cl_2$ (2 ml) at 0 °C was added *m*-CPBA (50–60%, 36.8 mg, 0.11 mmol). After stirring for 26 h at rt, the reaction mixture was quenched with $Na_2SO_3$ (22 mg) and the resulting mixture stirred for 30 min. The reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**15** (8 mg, 15.5%) and D-**16** (33 mg, 64.2%); *Method B*: To a solution of D-**13** (50 mg, 88.9 μmol) in dioxane/water (10:1, 1.5 ml) at rt were added NBS (or NIS) (0.178 mmol) and one drop of 0.1 M HCl. After stirring overnight at rt, the reaction mixture was diluted with EtOAc and washed with 5% aq $Na_2S_2O_3$, and satd aq $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated to give the crude mixture of bromohydrins (or iodohydrins). To this crude mixture in MeOH (3 ml) was added NaOME (85 μl, 25% in MeOH). After stirring for 6 h at rt the reaction mixture was extractively worked up with EtOAc, and chromatographed on silica gel column to give D-**15** and D-**16** (8 mg and 32 mg for NBS, 4 mg and 40 mg for NIS); *Method C*: To a solution of D-**3d** (62 mg, 103.9 μmol) in $CH_2Cl_2$ (1 ml) at rt were added $(MeO)_3CCH_3$ (20 μl, 158 μmol) and a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS, ca. 0.01 equiv). After stirring for 40 min at rt, the reaction mixture was treated with one drop of $Et_3N$ and concentrated and dried in vacuo. To the residue dissolved in $CH_2Cl_2$ (1 ml) at 0 °C were added one drop of $Et_3N$ and AcBr (29 mg, 2.35 equiv). After stirring for 4 h at rt, the reaction mixture was extractively worked up with $CH_2Cl_2$ to give a crude mixture of bromo acetoxy compound. To the crude mixture in MeOH (2 ml) at rt was added NaOMe (70 μl, 25% in MeOH). After stirring for 30 min, the reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**15** (51 mg, 84.7%) with the starting material D-**3d** (6.2 mg, 10%). D-**15**: $[\alpha]_D^{21} = +3.1$ (*c* 1.17, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.10 (s, 9H, –C(C$H_3$)$_3$), 1.74 (m, 1H, H-5), 2.0–2.2 (m, 2H, H-5a$_{ax}$ and H-5a$_{eq}$), 3.31 (t, $J = 4.1$ Hz, 1H, H-1), 3.35 (dd, $J = 4.0$, 1.7 Hz, 1H, H-2), 3.67 (dd, $J = 10.0$, 2.8 Hz, 1H, H-6$_\alpha$), 3.72 (dd, $J = 10.9$, 8.2 Hz, 1H, H-4), 3.83 (dd, $J = 10.3$, 5.25 Hz, 1H, H-6$_\beta$), 3.85 (dd, $J = 8.3$, 1.7 Hz, 1H, H-3), 4.5–4.9 (m, 4H, 2 × –OC$H_2$Ph), 7.1–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.4, 27.7, 30.4, 42.4, 54.2, 56.1, 63.9, 73.2, 75.8, 82.5, 128.1, 128.4, 128.6, 129.0, 129.1, 130.3, 134.1, 134.3, 136.4, 136.5, 139.2, 139.3; MS (FAB) *m/z* 579 ($M^+$+1), 601 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{42}O_4SiNa$ 601.2750 found 601.2748 ($M^+$+Na); D-**16**: $[\alpha]_D^{21} = -26.0$ (*c* 0.64, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C(C$H_3$)$_3$), 1.67 (m, 1H, H-5), 2.15 (m, 2H, H-5a$_{ax}$ and H-5a$_{eq}$), 3.21 (t, $J = 3.7$ Hz, 1H, H-2), 3.30 (m, 1H, H-2), 3.51 (dd, $J = 11.3$, 8.1 Hz, 1H, H-4), 3.59 (dd, $J = 9.9$, 2.4 Hz, 1H, H-6$_\alpha$), 3.81 (d, $J = 8.0$ Hz, 1H, H-4), 4.01 (dd, $J = 9.9$, 4.1 Hz, 1H, H-6$_\beta$), 4.60–4.91 (m, 4H, 2 × –OC$H_2$Ph), 7.1–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 28.2, 35.4, 53.89, 53.91, 63.5, 73.4, 75.1, 79.8, 81.7, 128.0, 128.3, 128.6, 128.7, 128.9, 129.2, 130.3, 130.4, 134.0, 134.1, 136.3, 136.4, 138.5, 139.4; MS (FAB) *m/z* 579 ($M^+$+1), 601 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{42}O_4SiNa$ 601.2750 found 601.2752 ($M^+$+Na).

### 4.20. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-mannopyranose, D-17

To a solution of D-**15** (20 mg, 34.5 μmol) in acetone (3 ml) at 0 °C was added $HClO_4$ (0.3 M, 53 μl, 15.9 μmol). After stirring for 8 h at 0 °C, the reaction mixture was quenched with $Na_2SO_3$ (10 drops) and the resulting mixture extractively worked up with EtOAc and chromatographed on silica gel to give D-**17** (19.5 mg, 94.6%) as a colorless oil. D-**17**: $[\alpha]_D^{21} = +3.0$ (*c* 0.44, $CHCl_3$); $^1$H NMR (acetone-$d_6$) $\delta$ 1.07 (s, 9H, –C(C$H_3$)$_3$), 1.75 (m, 1H, H-5$_{eq}$), 2.0 (m, 2H, H-5a$_{ax}$ and H-5), 3.76 (dd, $J = 9.8$, 2.2 Hz, 1H, H-6$_\alpha$), 3.83 (dd, $J = 8.8$, 2.8 Hz, 1H, H-3), 3.90 (t, $J = 9.1$ Hz, 1H, H-4), 3.96 (dd, $J = 9.6$, 4.7 Hz, 1H, H-6$_\beta$), 4.0 (m, 1H, H-1), 4.16 (pseudo t, $J = 2.8$ Hz, 1H, H-2), 4.52–4.93 (m, 4H, 2 × –OC$H_2$Ph), 7.1–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 30.4, 39.8, 64.4, 69.4, 72.6, 73.4, 74.9, 77.2, 82.4, 128.2, 128.3, 128.38, 128.43, 128.6, 129.0, 129.2, 130.3, 134.3, 134.4, 136.36, 136.41, 138.8, 139.4; MS (FAB) *m/z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2860 ($M^+$+Na).

### 4.21. Bromohydrins D-18 and D-19 from D-16

To a solution of D-**16** (10 mg, 17 μmol) in THF (0.5 ml) at rt were added AcOH (30 mg, 0.5 mmol) and LiBr (80 mg, 0.92 mmol). After stirring overnight, the reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**18** (7 mg, 61.4%) and D-**19** (3 mg, 26.3%). D-**18**: $^1$H NMR ($CDCl_3$) $\delta$ 1.10 (s, 9H, –C(C$H_3$)$_3$), 1.65 (m, 1H, H-5), 2.0 (app. q, $J = 13.1$ Hz, 1H, H-5a$_{ax}$), 2.28 (dt, $J = 13.4$, 4.0 Hz, 1H, H-5$_{eq}$), 2.67 (d, $J = 2.1$ Hz, 1H, –OH), 3.40 (t, $J = 9.0$ Hz, 1H, H-3), 3.59 (app t, $J = 10.5$ (9.3) Hz, 1H, H-4), 3.69 (app ddd, $J = 10.0$, 9.0, 2.1 Hz, 1H, H-2), 3.71 (dd, $J = 10.0$, 2.4 Hz, 1H, H-6$_\alpha$), 3.82–3.92 (m, 2H, H-1 and H-6$_\beta$), 4.53–4.90 (m, 4H, 2 × –OC$H_2$Ph), 7.0–7.65 (m, 20H, 4Ph); MS (FAB) *m/z* 659 ($M^+$+1), 681 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{43}BrO_4SiNa$ 659.2192 found 659.2192 ($M^+$+1). D-**19**: $^1$H NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C(C$H_3$)$_3$), 1.72 (dt, $J = 14.1$, 4.8 Hz, 1H, H-5$_{eq}$), 2.14 (m, 1H, H-5), 2.40 (ddd, $J = 13.8$, 9.6, 3.0 Hz, 1H, H-5a$_{ax}$), 3.69 (dd,

$J = 10.0$, 4.0 Hz, 1H, H-6$_\alpha$), 3.8–4.0 (m, 3H, H-3, H-4, and H-6$_\beta$), 4.18 (m, 1H, H-1), 4.39 (m, 1H, H-2), 4.5–4.82 (m, 4H, 2 × –OC$H_2$Ph), 7.1–7.7 (m, 20H, 4Ph); MS (FAB) *m/z* 659 ($M^+$+1), 681 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{43}BrO_4SiNa$ 659.2192 found 659.2193 ($M^+$+1).

### 4.22. 6-*O*-(*tert*-Butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-idopyranose, D-4b

To a solution of D-**4a** (1.5 g, 2.46 mmol) in MeOH (15 ml) was added NaOMe (0.739 mmol, 169 μl of 25% solution in MeOH). After stirring for 5 h at rt, the reaction mixture was treated with AcOH (44 mg) and concentrated. The residue was extractively worked up with EtOAc and chromatographed on silica gel to give D-**4b** (1.17 g, 94.1%) as a colorless oil. D-**4b**: $[\alpha]_D^{21} = -31.8$ (*c* 1.58, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.07 (s, 9H, –C(C$H_3$)$_3$), 1.64 (dt, $J = 13.7$, 4.4 Hz, 1H, H-5a$_{eq}$), 1.72 (m, 1H, H-5a$_{ax}$), 2.30 (m, 1H, H-5), 2.61 (br s, 1H, –OH), 3.30 and 3.44 (2s, 6H, 2 × –OCH$_2$OC$H_3$), 3.65 (dd, $J = 10.0$, 6.2 Hz, 1H, H-6α), 3.67 (m, 1H), 3.80 (m, 2H), 3.99 (dt, $J = 8.2$, 3.5 Hz, 1H), 4.04–4.15 (m, 2H), 4.6–4.8 (m, 4H, 2 × –OC$H_2$OCH$_3$), 7.3-7.7 (m, 10H, 2Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.9, 26.2, 27.5, 39.6, 56.1, 56.6, 61.1, 66.0, 71.6, 73.2, 73.8, 79.4, 96.0, 97.6, 128.4, 130.4, 134.1, 134.2, 136.3; MS (FAB) *m/z* 527 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{27}H_{40}O_7$SiNa 527.2441 found 527.2445 ($M^+$+Na).

### 4.23. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-idopyranose, D-4c

To a solution of D-**4b** (1.00 g, 1.981 mmol) in dry THF (35 ml) at 0 °C was added NaH (518 mg, 55% in paraffin liquid, 11.9 mmol). After stirring for 30 min at rt, BnBr (1.41 ml, 11.9 mmol) and $Bu_4NI$ (146 mg, 0.396 mmol) were added. After stirring for 24 h at rt, the reaction mixture was quenched with drops of satd aq $NaHCO_3$ and worked up by a standard extractive procedure. The crude product was chromatographed on silica gel to give compound D-**4c** (1.06 g, 78%) as a colorless oil. D-**4c**: $[\alpha]_D^{21} = -7.1$ (*c* 1.78, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.10 (s, 9H, –C(C$H_3$)$_3$), 1.46 (pseudo d, $J = 13.0$ Hz, 1H, H-5a$_{eq}$), 2.1 (m, 1H, H-5a$_{ax}$), 2.28 (m, 1H, H-5), 3.37 and 3.41 (2s, 6H, 2 × –OCH$_2$OC$H_3$), 3.74 (pseudo t, $J = 3.9$ Hz, 1H), 3.80–3.93 (m, 4H), 4.02 (m, 1H), 4.39–4.81 (m, 8H, 2 × –OC$H_2$Ph, 2 × –OC$H_2$OCH$_3$), 7.2–7.71 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.7, 24.5, 27.3, 39.4, 55.8, 55.9, 64.1, 72.4, 73.6 (2s), 76.2, 76.8, 95.0, 97.1, 127.8, 128.0, 128.16, 128.20, 128.6, 128.8, 130.0, 134.2, 134.3, 136.0, 138.8, 139.1; MS (FAB) *m/z* 707 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{41}H_{52}O_7$SiNa 707.3380 found 707.3376 ($M^+$+Na).

### 4.24. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-idopyranose, D-4d

To a solution of D-**4c** (915 mg, 1.34 mmol) and molecular sieves 4 Å (2 g, powder) in dry $CH_2Cl_2$ (9 ml) at −20 °C was added TMSBr (2.69 ml, 20.0 mmol). After stirring for 2 h at −20 °C, the reaction mixture was poured into satd aq $NaHCO_3$. After filtering the resulting mixture on Celite, the filtrate was extractively worked up with EtOAc and chromatographed on silica gel to give compound D-**4d** (550 mg, 69%) as a colorless oil. D-**4d**: $[\alpha]_D^{21} = +7.2$ (*c* 1.08, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (s, 9H, –C(C$H_3$)$_3$), 1.39 (app q, $J =$ 12.4 Hz, 1H, H-5a$_{ax}$), 1.58 (dt, $J = 12.7$, 4.2 Hz, 1H, H-5a$_{eq}$), 2.24 (m, 1H, H-5), 3.61 (dd, $J = 9.8$, 5.9 Hz, 1H, H-6$_\alpha$), 3.77 (t, $J = 9.6$ Hz, 1H, H-6$_\beta$), 3.87 (ddd, $J = 11.4$, 4.7, 3.2 Hz, 1H, H-1), 3.95 (t, $J = 3.3$ Hz, 1H, H-3 or H-4), 3.99 (br s, 1H, H-4 or H-3), 4.02 (br s, 1H, H-2), 4.4–4.7 (m, 4H, 2 × –OC$H_2$Ph), 7.2–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.2, 27.6, 38.7, 64.7, 68.5, 72.5, 72.8, 74.4, 75.2, 76.2, 128.3, 128.4, 128.6, 128.8, 128.9, 129.2, 129.3, 130.4, 130.5, 134.1, 134.3, 136.26, 136.30, 137.9, 138.5; MS (FAB) *m/z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{37}H_{44}O_5$SiNa 619.2856 found 619.2861 ($M^+$+Na).

### 4.25. 1-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-idopyranose, D-4e and 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-idopyranose, D-4f

*Method A*: To a solution of D-**4d** (80 mg, 0.134 mmol) in dry THF (2 ml) at rt were added sequentially $Et_3N$ (37.4 μl, 0.268 mmol) and $Me_2SnCl_2$ (1.5 mg, 7.0 μmol, 5.4 mol %). To the resulting mixture at 0 °C was added dropwise BzCl (18.7 μl, 0.161 mmol) in THF (0.1 ml). After stirring for 6 h at rt, the reaction mixture was quenched with $H_2O$ (three drops), extractively worked up with EtOAc, and chromatographed on silca gel to give D-**4e** (89.6 mg, 0.128 mmol, 91.9%) and D-**4f** (5.9 mg, 0.008 mmol, 6.0%) as an oil; *Method B*: To a solution of D-**4d** (100 mg, 0.167 mmol) in $CH_2Cl_2$ (2 ml) were added $(EtO)_3CPh$ (76 μl, 0.335 mmol) and TSA (ca. 1 mg, 5.0 μmol) at rt. After stirring for 30 min, the reaction mixture was concentrated by evaporation and the resulting residue was treated with 80% aq AcOH (1 ml) and stirred for 10 min at rt. The resulting mixture was extractively worked up with EtOAc, and chromatographed on silica gel column to give compounds D-**4e** (14.6 mg, 12.3%) and D-**4f** (86.6 μg, 73.1%) as colorless oils. D-**4e**: $[\alpha]_D^{21} = +0.3$ (*c* 1.25, $CHCl_3$); $^1$H NMR ($CDCl_3$ with $D_2O$ one drop) $\delta$ 1.08 (s, 9H, –C(C$H_3$)$_3$), 1.64 (dt, $J = 12.7$, 4.0 Hz, 1H, H-5a$_{eq}$), 1.78 (app q, $J = 12.4$ Hz, 1H, H-5a$_{ax}$), 2.40 (m, 1H, H-5), 3.61 (dd, $J = 9.8$, 5.9 Hz, 1H, H-6$_\alpha$), 3.80 (t, $J = 9.7$ Hz, 1H, H-6$_\beta$), 3.96 (t, $J = 3.4$ Hz, 1H, H-3 or H-4), 4.06 (br s, 1H, H-4 or H-3), 4.26 (br s, 1H, H-2), 4.4–4.7 (m, 4H, 2 × –OC$H_2$Ph), 5.32 (ddd, $J = 11.8$, 4.7, 3.2 Hz, 1H, H-1), 7.2–8.1 (m, 25H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 23.2, 27.6, 38.9, 64.5, 70.6, 72.7, 72.9, 74.4, 75.2, 76.4, 128.5, 128.6, 128.8, 128.9, 129.0, 129.2, 129.3, 130.4, 130.5, 131.2, 133.5, 134.0, 134.3, 136.3, 137.8, 138.5, 166.8 (Ph*C*=O); MS (FAB) *m/z* 701 ($M^+$+1), 723 ($M^+$+Na); HRMS (FAB) *m/z* calcd for $C_{44}H_{48}O_6$SiNa 723.3118 found 723.3112 ($M^+$+Na); D-**4f**: $[\alpha]_D^{21} = -24.8$ (*c* 0.89, $CHCl_3$); $^1$H NMR ($CDCl_3$ with $D_2O$ one drop) $\delta$ 1.11 (s, 9H, –C(C$H_3$)$_3$), 1.67 (dt, $J = 12.5$, 4.0 Hz, 1H, H-5a$_{eq}$), 1.88 (app q, $J = 11.8$ Hz, 1H, H-5a$_{ax}$), 2.30 (m, 1H, H-5), 3.75 (dd, $J = 9.4$, 6.1 Hz, 1H, H-6$_\alpha$), 3.88 (br s, 1H, H-3 or H-

4), 3.91 (t, $J = 9.6$ Hz, 1H, H-6$_\beta$), 4.15 (t, $J = 3.7$ Hz, H-4 or H-3), 4.19 (m, 1H, H-1), 4.3–4.8 (m, 4H, 2 × –OC$H_2$Ph), 5.43 (pseudo t, $J = 3.3$ Hz, 1H, H-2), 7.2–8.0 (m, 25H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.6, 28.4, 39.5, 64.9, 68.4, 73.2, 73.7, 73.9, 75.0, 75.9, 128.1, 128.4, 128.5, 128.8, 129.0, 129.2, 130.3, 130.6, 130.7, 133.7, 134.2, 136.3, 136.4, 138.6, 138.9, 167.3 (Ph*C*=O); MS (FAB) *m*/*z* 701 ($M^+$+1), 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3120 ($M^+$+Na).

### 4.26. (2*R*,4*S*,5*S*,6*R*)-2-Benzoyloxy-4-(*tert*-butyl-diphenyl-silanyloxymethyl)-5,6-di-benzyloxy-cyclohexanone, D-20

To a stirred mixture of D-**4e** (63 mg, 89.9 μmol) and molecular sieves 4 Å (powder, 100 mg) in $CH_2Cl_2$ (4 ml) at rt was added PCC (58.1 mg, 0.27 mmol). After stirring for 7 h, the reaction mixture was filtered through a silica gel column and washed with EtOAc/*n*-hexane (1:4). The filtrate was concentrated to give D-**20** (61.2 mg, 87.6 μmol, 97.4%) as a colorless oil. D-**20**: $[\alpha]_D^{21} = -24.7$ (*c* 1.025, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.06 (s, 9H, –C(C$H_3$)$_3$), 2.00 (app q, $J = 12.5$ Hz, 1H, H-3$_{ax}$), 2.13 (m, 1H, H-3$_{eq}$), 2.77 (m, 1H, H-4), 3.62 (dd, $J = 9.7$, 6.5 Hz, 1H, H-7$_\alpha$), 3.77 (t, $J = 9.6$ Hz, 1H, H-7$_\beta$), 4.08 (d, $J = 3.7$ Hz, 1H, H-6), 4.18 (br s, 1H, H-5), 4.38–4.83 (m, 4H, 2 × –OC$H_2$Ph), 5.93 (dd, $J = 12.5$, 6.8 Hz, 1H, H-2), 7.2–8.1 (m, 25H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.8, 27.4, 30.2, 38.5, 64.0, 72.7, 73.0, 74.3, 78.8, 81.3, 128.3, 128.66, 128.74, 128.85, 128.89, 129.1, 130.1, 130.2, 130.3, 130.4, 133.7, 133.9, 134.0, 136.08, 136.12, 137.4, 138.2, 166.2 (Ph*C*=O), 204.7 (C-1); MS (FAB) *m*/*z* 699 ($M^+$+H), 721 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{46}O_6SiNa$ 721.2961 found 721.2969 ($M^+$+Na).

### 4.27. 1-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-diphenyl)silyl-5a-carba-β-D-gulopyranose, D-21

To a solution of D-**20** (41 mg, 58.7 μmol) in $CH_2Cl_2$/MeOH (4.8 ml) and at −20 °C was added $NaBH_4$ (7.0 mg, 0.185 mmol). After stirring for 30 min at −20 °C, the reaction mixture was treated with AcOH (three drops) and stirred for an additional 10 min. The reaction mixture was filtered on silica gel pad and the filtrate was concentrated to give a mixture of (D-**21**/D-**4e** ~ 43:57). This mixture was chromatographed to give D-**21** ($R_f = 0.60$ in TLC with EtOAc/*n*-hexane = 1:7, 15.6 mg, 37.9%) and D-**4e** ($R_f = 0.72$ in TLC with EtOAc/*n*-hexane = 1:7, 21.1 mg, 51.4%). D-**21**: $[\alpha]_D^{20} = -42.7$ (*c* 0.97, $CHCl_3$); $^1$H NMR ($CDCl_3$ with $D_2O$ one drop) $\delta$ 1.08 (s, 9H, –C(C$H_3$)$_3$), 1.56 (app q, $J = 12.4$ Hz, 1H, H-5a$_{ax}$), 1.76 (dt, $J = 12.2$, 4.1 Hz, 1H, H-5a$_{eq}$), 2.35 (m, 1H, H-5), 3.60 (dd, $J = 9.8$, 5.7 Hz, 1H, H-6$_\alpha$), 3.79 (t, $J = 9.7$ Hz, 1H, H-6$_\beta$), 3.98 (t, $J = 3.5$ Hz, 1H, H-3), 4.03 (dd, $J = 9.7$, 3.4 Hz, 1H, H-2), 4.12 (br s, 1H, H-4), 4.5–4.7 (m, 4H, 2 × –OC$H_2$Ph), 5.27 (ddd, $J = 11.3$, 9.8, 5.0 Hz, 1H, H-1), 7.2–8.1 (m, 25H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.6, 38.3, 64.3, 72.5, 73.80, 73.82, 74.4, 74.8, 78.9, 128.4, 128.5, 128.66, 128.74, 129.0, 129.1, 129.3, 130.4, 130.5, 131.1, 133.6, 134.1, 134.3, 136.2, 138.5, 139.0, 167.5 (Ph*C*=O); MS (FAB) *m*/*z* 701 ($M^+$+1), 723 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{44}H_{48}O_6SiNa$ 723.3118 found 723.3120 ($M^+$+Na).

### 4.28. 1,2-Anhydro-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-diphenyl)silyl-5a-carba-β-D-idopyranose, D-22

To a solution of D-**4d** (153 mg, 0.260 mmol) in $CH_2Cl_2$ (3 ml) at rt were added $(MeO)_3CCH_3$ (51 μl, 0.40 mmol) and a catalytic amount of PPTS (ca. 0.01 equiv). After stirring for 40 min at rt, the reaction mixture was treated with one drop of $Et_3N$ and concentrated and dried in vacuo. To the residue dissolved in $CH_2Cl_2$ (3 ml) at 0 °C were added two drops of $Et_3N$ and AcBr (77.1 mg, 0.627 mmol). After stirring for 4 h at rt, the reaction mixture was poured into satd aq $NaHCO_3$ and extractively worked up with $CH_2Cl_2$ to give a crude mixture of bromo acetoxy compounds. To the crude mixture in MeOH (5 ml) at rt was added NaOMe (178 μl, 25% in MeOH). After stirring for 30 min, the reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**22** (106.2 mg, 70.7%) with the starting material D-**4d** (38.4 mg, 24.8%). D-**22**: $[\alpha]_D^{21} = +30.3$ (*c* 0.94, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C(C$H_3$)$_3$), 1.84 (ddd, $J = 18.2$, 9.0, 4.2 Hz, 1H, H-5a$_{ax}$), 2.17 (m, 2H, H-5 and H-5a$_{eq}$), 3.17 (d, $J = 3.6$ Hz, 1H, H-2), 3.25 (t, $J = 3.7$ Hz, 1H, H-1), 3.65–3.83 (m, 4H, H-3, H-4, H-6$_\alpha$, H-6$_\beta$), 4.49–4.65 (m, 4H, 2 × –OC$H_2$Ph), 7.27–7.7 (m, 20H, 5Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.8, 23.2, 27.5, 36.2, 52.6, 53.9, 64.1, 72.4, 73.4, 74.2, 76.9, 128.1, 128.2, 128.4, 128.8, 129.0, 130.1, 134.3, 134.5, 136.10, 136.14, 138.5, 139.1; MS (FAB) *m*/*z* 579 ($M^+$+1), 601 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{42}O_4SiNa$ 601.2750 found 601.2745 ($M^+$+Na).

### 4.29. 1-*O*-Allyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-diphenyl)silyl-5a-carba-α-D-idopyranose, D-23

To a solution of D-**22** (26.8 mg, 46.3 μmol) in allyl alcohol (1.5 ml) at rt was added TSA (2.3 mg, 0.26 equiv). After stirring for 3.5 h at rt, $Et_3N$ (two drops) was added and the resulting mixture concentrated by co-evaporation with EtOAc (5 ml × 3). The residue was chromatographed on silica gel column to give D-**23** (21.6 mg, 73.2%). D-**23**: $[\alpha]_D^{20} = +19.3$ (*c* 1.05, $CHCl_3$); $^1$H NMR (acetone-$d_6$) $\delta$ 1.09 (s, 9H, –C(C$H_3$)$_3$), 1.40 (ddd, $J = 13.4$, 11.2, 4.8 Hz, 1H, H-5a$_{ax}$), 2.40 (dt, $J = 13.4$, 4.4 Hz, 1H, H-5a$_{eq}$), 2.5 (m, 1H, H-5), 3.52 (td, $J = 8.7$, 3.7 Hz, 1H, H-2), 3.68–3.71 (m, 2H, H-3, H-4), 3.75 (ddd, $J = 11.2$, 8.7, 4.7 Hz, 1H, H-1), 3.90 (m, 2H, H-6$_\alpha$ and H-6$_\beta$), 4.09 (d, $J = 3.6$ Hz, 1H, –OH), 4.18–4.21 (m, 2H, –OC$H_2$CH=CH$_2$), 4.55 (s, 2H, –OC$H_2$Ph), 4.81 (s, 2H, –OC$H_2$Ph), 5.10 (pseudo dd, $J = 10.5$, 1.7 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.31 (ddd, $J = 17.2$, 3.5, 1.7 Hz, 1H, –OCH$_2$CH=CH$_\alpha$H$_\beta$), 5.97 (m, 1H, –OCH$_2$C*H*=CH$_2$), 7.1–7.72 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.7, 27.5, 27.7, 37.4, 62.6, 71.3, 72.7, 75.3, 76.7, 77.0, 81.3, 81.8, 117.5, 128.1, 128.3, 128.4, 128.86, 128.93, 130.2, 130.3, 133.8, 134.0, 135.8,

136.2, 138.7, 139.4; MS (FAB) $m/z$ 637 ($M^+$+1), 659 ($M^+$+Na); HRMS (FAB) $m/z$ calcd for $C_{40}H_{48}O_5SiNa$ 659.3169 found 659.3165 ($M^+$+Na).

### 4.30. (2*R*,3*S*,4*S*,6*R*)-6-Allyloxy-4-(*tert*-butyl-diphenyl-silanyloxymethyl)-2,3-di-benzyloxy-cyclohexanone, D-24

To a stirred mixture of D-**23** (18 mg, 28.3 μmol) and molecular sieves 4 Å (powder, 30 mg) in $CH_2Cl_2$ (1 ml) at rt was added PCC (18.3 mg, 84.8 μmol). After stirring for 3.5 h, the reaction mixture was filtered through a silica gel column and washed with EtOAc/*n*-hexane (1:3). The filtrate was concentrated to give D-**24** (17.9 mg, 28.2 μmol, 99.8%) as a colorless oil. D-**24**: $[\alpha]_D^{21}$ = +12.8 (*c* 0.9, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.03 (s, 9H, –C(C$H_3$)$_3$), 1.68 (ddd, $J$ = 13.2, 11.7, 5.0 Hz, H-5$_{ax}$), 2.44 (m, 2H, H-5$_{eq}$ and H-4), 3.82 (dd, $J$ = 9.1, 5.6 Hz, 1H, H-3), 3.87 (dd, $J$ = 10.4, 3.7 Hz, 1H, H-7$_\alpha$), 3.99 (pseudo dd, $J$ = 12.8, 6.0 Hz, 1H, –OC$H_\alpha$H$_\beta$-CH=CH$_2$), 4.11 (dd, $J$ = 10.1, 5.7 Hz, 1H, H-7$_\beta$), 4.28 (dd, $J$ = 12.8, 5.3 Hz, 1H, –OCH$_\alpha$$H_\beta$CH=CH$_2$), 4.51 (dd, $J$ = 12.4, 6.9 Hz, 1H, H-6), 4.53–4.91 (m, 5H, H-2 and 2 × –OC$H_2$Ph), 5.20 (pseudo dd, $J$ = 10.3, 1.2 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.30 (pseudo dd, $J$ = 17.2, 1.5 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.97 (1H, –OCH$_2$-C$H$=CH$_2$), 7.1–7.72 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.8, 27.6, 32.0, 37.9, 63.8, 71.9, 73.9, 74.1, 79.2, 82.5, 85.4, 118.2, 128.27, 128.34, 128.47, 128.51, 129.01, 129.03, 130.5, 130.6, 133.5, 133.7, 135.2, 136.3, 136.4, 138.7, 139.0, 206.2 (C-1); MS (FAB) $m/z$, 657 ($M^+$+Na); HRMS (FAB) $m/z$ calcd for $C_{40}H_{46}O_5SiNa$ 657.3012 found 657.3021 ($M^+$+Na).

### 4.31. 1-*O*-Allyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-gulopyranose, D-25

To a solution of D-**24** (14.4 mg, 22.7 μmol) in THF (1.5 ml) at −20 °C was added L-Selectride™ (113 μl, 1 M solution in THF). After stirring for 20 min, the reaction mixture was quenched by several drops of satd aq $NaHCO_3$, and was extractively worked up with EtOAc, and purified by silica gel column chromatography to give D-**25** (10.6 mg, 73.4%). D-**25**: $[\alpha]_D^{19}$ = +17.2 (*c* 0.53, $CHCl_3$); $^1$H NMR ($C_6D_6$ with $D_2O$ drop) $\delta$ 1.26 (s, 9H, –C(C$H_3$)$_3$), 1.64 (br t, $J$ = 12.5 (10.8) Hz, 1H, H-5a$_{ax}$), 1.78 (br d, $J$ = 13.7 Hz, 1H, H-5a$_{eq}$), 2.66 (m, 1H, H-5), 3.72 (pseudo q, $J$ = 3.4 Hz, 1H, H-1), 3.81 (dd, $J$ = 9.8, 6.7 Hz, 1H, H-6$_\alpha$), 3.84 (dd, $J$ = 9.8, 5.3 Hz, 1H, H-6$_\beta$), 3.9–4.03 (m, 3H, H4, OC$H_2$CH=CH$_2$), 4.11 (t, $J$ = 3.5 Hz, 1H, H-2), 4.15 (t, $J$ = 3.7 Hz, 1H, H-3), 4.38–4.70 (m, 4H, 2 × –OC$H_2$Ph), 5.12 (pseudo dd, $J$ = 10.4, 1.5 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.37 (pseudo dd, $J$ = 17.2, 1.7 Hz, 1H, –OCH$_2$CH=CH$_\alpha$$H_\beta$), 5.92 (m, 1H, –OCH$_2$-C$H$=CH$_2$), 7.1–7.9 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.9, 25.8, 27.6, 34.9, 64.3, 69.3, 71.1, 73.3, 73.7, 76.2, 76.6, 78.2, 117.2, 128.18, 128.24, 128.28, 128.35, 128.4, 128.97, 129.01, 130.3, 134.2, 134.4, 136.0, 136.28, 136.3, 139.3, 139.4; MS (FAB) $m/z$ 637 ($M^+$+1), 659 ($M^+$+Na); HRMS (FAB) $m/z$ calcd for $C_{40}H_{48}O_5SiNa$ 659.3169 found 659.3169 ($M^+$+Na).

### 4.32. 6-*O*-(*tert*-Butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-talopyranose, D-5b

To a solution of D-**5a** (1.5 g, 2.46 mmol) in MeOH (15 ml) was added NaOMe (0.739 mmol, 169 μl of 25% solution in MeOH). After stirring for 4.5 h at rt, the reaction mixture was treated with AcOH (44 mg) and concentrated. The residue was extractively worked up with EtOAc and chromatographed on silica gel to give D-**5b** (1.18 g, 94.8%) as a colorless oil. D-**5b**: $[\alpha]_D^{18}$ = −26.1 (*c* 1.0, $CHCl_3$); $^1$H NMR (acetone-$d_6$ with one drop of $D_2O$) $\delta$ 1.04 (s, 9H, –C(C$H_3$)$_3$), 1.58 (app q, $J$ = 12.5 Hz, 1H, H-5a$_{ax}$), 1.68 (dt, $J$ = 12.4, 4.3 Hz, 1H, H-5a$_{eq}$), 1.80 (m, 1H, H-5), 3.33 and 3.41 (2s, 6H, 2 × –OCH$_2$OC$H_3$), 3.56 (m, 1H, H-3), 3.63 (dd, $J$ = 9.5, 6.4 Hz, 1H, H-6$_\alpha$), 3.8 (ddd, $J$ = 11.6, 4.8, 2.5 Hz, 1H, H-1), 3.90 (dd, $J$ = 9.5, 8.0 Hz, 1H, H-6$_\beta$), 3.98 (br s, 1H, H-4), 4.19 (br s, 1H, H-2), 4.60–4.85 (m, 4H, 2 × –OC$H_2$OCH$_3$), 7.4–7.8 (m, 10H, 2Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.9, 23.8, 27.5, 41.5, 56.2, 57.0, 65.0, 70.9, 71.5, 75.3, 82.1, 95.4, 99.1, 128.4, 130.3, 134.3, 134.5, 136.26, 136.32; MS (FAB) $m/z$ 505 ($M^+$+1), 527 ($M^+$+Na); HRMS (FAB) $m/z$ calcd for $C_{27}H_{40}O_7SiNa$ 527.2441 found 527.2441 ($M^+$+Na).

### 4.33. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-1,2-di-*O*-(methoxymethyl)-5a-carba-β-D-talopyranose, D-5c

To a solution of D-**5b** (1.00 g, 1.981 mmol) in dry THF (35 ml) at 0 °C was added NaH (518 mg, 55% in paraffin liquid, 11.9 mmol). After stirring for 30 min at rt, BnBr (1.41 ml, 11.9 mmol) and $Bu_4NI$ (146 mg, 0.396 mmol) were added. After stirring for 3 days at rt, the reaction mixture was quenched with drops of satd aq $NaHCO_3$, extractively worked up with EtOAc, and chromatographed on silica gel to give compound D-**5c** (1.28 g, 94.3%) as a colorless oil. D-**5c**: $[\alpha]_D^{20}$ = −2.6 (*c* 1.21, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.04 (s, 9H, –C(C$H_3$)$_3$), 1.46 (md, $J$ = 11.7 Hz, 1H, H-5a$_{eq}$), 1.60 (m, 1H, H-5), 1.86 (app q, $J$ = 12.1 Hz, 1H, H-5a$_{ax}$), 3.26 (s, 1H, H-3), 3.37 and 3.39 (2s, 6H, 2 × –OCH$_2$OC$H_3$), 3.55 (m, 2H, H-1, H-6$_\alpha$), 3.78 (t, $J$ = 8.4 Hz, 1H, H-6$_\beta$), 4.10 (s, 1H, H-2), 4.37 (s, 1H, H-4), 4.5–5.1 (m, 8H, 2 × –OC$H_2$Ph, 2 × –OC$H_2$OCH$_3$), 7.2–7.62 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.8, 25.0, 27.4, 41.4, 56.0, 65.1, 71.4, 73.6, 74.3, 74.6, 75.3, 81.8, 94.8, 97.6, 127.4, 127.7, 128.1, 128.17, 128.21, 128.5, 128.9, 130.1, 130.2, 134.23, 134.29, 136.1, 139.0, 140.5; MS (FAB) $m/z$ 707 ($M^+$+Na); HRMS (FAB) $m/z$ calcd for $C_{41}H_{52}O_7SiNa$ 707.3380 found 707.3383 ($M^+$+Na).

### 4.34. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-talopyranose, D-5d

To a solution of D-**5c** (900 mg, 1.31 mmol) and molecular sieves 4 Å (2 g, powder) in dry $CH_2Cl_2$ (10 ml) at −20 °C was added TMSBr (3.46 ml, 26.2 mmol). After stirring for 3 h at −20 °C, the reaction mixture was poured into satd aq $NaHCO_3$. After filtering the resulting mixture on Celite, the filtrate was extractively worked up with EtOAc and chromatographed on silica gel to give compound D-**5d** (490 mg, 63%) as a colorless

oil. D-**5d**: $[\alpha]_D^{18} = -1.2$ (*c* 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$, with $D_2O$ one drop) $\delta$ 1.05 (s, 9H, –C($CH_3$)$_3$), 1.36 (app q, $J = 12.0$ Hz, 1H, H-5$a_{ax}$), 1.49 (dt, $J = 12.7$, 4.3 Hz, 1H, H-5$a_{eq}$), 1.58 (m, 1H, H-5), 3.29 (t, $J = 2.6$ Hz, 1H, H-3), 3.40 (m , 1H, H-1), 3.55 (dd, $J = 9.9$, 5.5 Hz, H, H-6$_\alpha$), 3.70 (t, $J = 9.7$ Hz, 1H, H-6$_\beta$), 4.18 (s, 1H, H-2), 4.23 (s, 1H, H-4), 4.52–5.03 (m, 4H, 2 × –O$CH_2$Ph), 7.2–7.63 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.8, 27.1, 27.5, 40.4, 64.4, 70.6 (2s), 72.5, 76.3, 78.2, 128.2, 128.31, 128.34, 128.4, 128.5, 129.0, 129.1, 130.31, 130.34, 133.9, 136.06, 136.08, 138.2, 138.5; MS (FAB) *m*/*z* 597 ($M^+$+1), 619 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2854 ($M^+$+Na).

### 4.35. 1,2-Anhydro-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-diphenyl)silyl-5a-carba-β-D-talopyranose, D-26

To a solution of D-**5d** (201.7 mg, 0.338 mmol) in $CH_2Cl_2$ (4 ml) at rt were added $(MeO)_3CCH_3$ (140 μl, 1.09 mmol) and a catalytic amount of PPTS (ca. 0.01 equiv). After stirring for 2 h at rt, the reaction mixture was treated with two drops of $Et_3N$, concentrated, and dried in vacuo. To the residue dissolved in $CH_2Cl_2$ (4 ml) at 0 °C were added three drops of $Et_3N$ and AcBr (103 mg, 0.838 mmol). After stirring for 3 h at rt, the reaction mixture was extractively worked up with $CH_2Cl_2$ to give a crude mixture of the bromo acetoxy compounds. To the crude mixture in MeOH (4 ml) was added NaOMe (230 μl, 25% in MeOH) at rt. After stirring for 50 min, the reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**26** (178.62 mg, 91.3%) with the starting material D-**5d** (16.3 mg, 8.1%). D-**26**: $[\alpha]_D^{20} = -11.5$ (*c* 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.06 (s, 9H, –C($CH_3$)$_3$), 1.6–1.8 (m, 3H, H-5, H-5$a_{ax}$, H-5$a_{eq}$), 3.31 (br s, 2H, H-1, H-2), 3.52 (dd, $J = 10.0$, 6.5 Hz, 1H, H-6$_\alpha$), 3.60 (dd, $J = 10.0$, 7.9 Hz, 1H, H-6$_\beta$), 3.77 (pseudo d, $J = 2.7$ Hz, 1H, H-3), 4.04 (br d, $J = 2.6$ Hz, 1H, H-4), 4.56–4.97 (m, 4H, 2 × –O$CH_2$Ph), 7.27–7.62 (m, 20H, 5Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.9, 23.1, 27.6, 41.6, 53.0, 53.2, 65.1, 71.5, 74.6, 75.1, 77.8, 127.8, 128.3, 128.4, 128.8, 129.1, 130.4, 134.3, 134.4, 136.2, 139.2, 140.1; MS (FAB) *m*/*z* 579 ($M^+$+1), 601 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{42}O_4SiNa$ 601.2750 found 601.2747 ($M^+$+Na).

### 4.36. 1-*O*-Allyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyl-diphenyl)silyl-5a-carba-α-D-talopyranose, D-27a

To a solution of D-**26** (21.5 mg, 37.1 μmol) in allyl alcohol (1.5 ml) at rt was added TSA (2.9 mg, 0.4 equiv) in portions. After stirring for 26 h at rt, $Et_3N$ (two drops) was added and the resulting mixture concentrated by co-evaporation with EtOAc (15 ml). The residue was filtered on a silica gel pad and the filtrate concentrated and chromatographed on silica gel column to give D-**27a** (16.0 mg, 67.6%). D-**27a**: $[\alpha]_D^{21} = +3.2$ (*c* 0.80, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C($CH_3$)$_3$), 1.45 (dt, $J = 13.9$, 2.7 Hz, 1H, H-5$a_{eq}$), 1.64 (td, $J = 13.7$, 2.3 Hz, 1H, H-5$a_{ax}$), 2.09 (m, 1H, H-5), 3.55 (dd, $J = 9.8$, 5.8 Hz, 1H, H-6$_\alpha$) 3.70 (pseudo t, $J = 2.3$ Hz, 1H, H-3), 3.72–3.79 (m, 2H, H-1 and H-6$_\beta$), 3.89–4.04 (m, 2H, –O$CH_2$CH=$CH_2$), 4.19 (br s, 1H, H-2), 4.33 (br s, 1H, H-4), 4.56–5.07 (m, 4H, 2 × –O$CH_2$Ph), 5.17 (dq, $J = 10.3$, 1.5 Hz, 1H, –O$CH_2$CH=C$H_\alpha H_\beta$), 5.31 (ddd, $J = 17.2$, 3.1, 1.6 Hz, 1H, –O$CH_2$CH=C$H_\alpha H_\beta$), 5.87 (m, 1H, –O$CH_2$C*H*=$CH_2$), 7.3–7.68 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.6, 22.0, 27.2, 38.2, 64.4, 70.35, 70.44, 70.6, 75.8, 76.5, 78.0, 78.4, 116.9, 127.9, 127.98, 128.03, 128.2, 128.68, 128.74, 130.00, 130.03, 133.9, 135.4, 135.9, 138.7, 139.4; MS (FAB) *m*/*z* 637 ($M^+$+1), 659 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{40}H_{48}O_5SiNa$ 659.3169 found 659.3173 ($M^+$+Na).

### 4.37. (1*R*,2*S*,3*S*)-1,2-Di-benzyloxy-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-cyclohex-5-ene, D-28

To a mixture of D-**26** (92.0 mg, 0.159 mmol) and $PPh_3$ (83.4 mg, 0.318 mmol) in DMF (1 ml) was added $I_2$ (resublimed, 80.7 mg, 0.318 mmol). After 25 min, Zn dust (52 mg, 0.795 mmol) was added to the mixture. After stirring for 1 h, the reaction mixture was directly loaded on a silica gel column and eluted with EtOAc/*n*-hexane (1:20) to give compound D-**28** (82.3 mg, 92.0%) as a colorless oil. D-**28**: $[\alpha]_D^{20} = -27.4$ (*c* 1.07, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.07 (s, 9H, –C($CH_3$)$_3$), 1.96 (m, 3H, H-3, H-4$a_{ax}$, H-4$a_{eq}$), 3.58 (pseudo dd, $J = 10.1$, 5.3 Hz, 1H, H-7$_\alpha$), 3.76 (dd, $J = 10.1$, 7.3 Hz, 1H, H-7$_\beta$), 4.11 (br s, 1H, H-2), 4.22 (m, 1H, H-1), 4.61–5.01 (m, 4H, 2 × –O$CH_2$Ph), 5.72 (pseudo d, $J = 10.2$ Hz, 1H, H-6, olefin), 5.79 (m, 1H, H-5, olefin), 7.27–7.66 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 20.0, 25.6, 27.6, 41.1, 65.2, 71.5, 74.2, 74.7, 78.2, 126.9, 127.8, 128.07, 128.13, 128.2, 128.3, 128.8, 129.0, 129.1, 130.3, 134.48, 134.53, 136.2, 139.6, 140.3; MS (FAB) *m*/*z* 563 ($M^+$+1), 585 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{42}O_3SiNa$ 585.2801 found 585.2802 ($M^+$+Na).

### 4.38. 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-galactopyranose, D-29

To a solution of D-**28** (20.4 mg, 36.3 μmol) and 4-methylmorpholine-*N*-oxide (NMO) (8.5 mg, 72.6 μmol) in acetone/water (2 ml, 8:1) at rt was added a catalytic amount of $OsO_4$. After stirring for 6 h, $Na_2SO_3$ (112 mg) was added and the resulting mixture was further stirred for 30 min at rt. The reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give compound D-**29** (19.8 mg, 91.4%) as a colorless oil. D-**29**: $[\alpha]_D^{18} = +46.9$ (*c* 1.0, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.09 (s, 9H, –C($CH_3$)$_3$), 1.55 (m, 2H, H-5$a_{ax}$, H-5$a_{eq}$), 2.23 (m, 1H, H-5), 2.59 (br s, 2H, 2 × –OH), 3.55 (dd, $J = 9.7$, 5.5 Hz, 1H, H-6$_\alpha$), 3.71 (dd, $J = 9.7$, 2.2 Hz, 1H, H-3), 3.74 (dd, $J = 9.7$ Hz, 1H, H-6$_\beta$), 4.07 (dd, $J = 9.7$, 3.2 Hz, 1H, H-2), 4.13 (pseudo q, $J = 3.0$ Hz, 1H, H-1), 4.38 (pseudo t, $J = 2.2$ Hz, 1H, H-4), 4.57–4.99 (m, 4H, 2 × –O$CH_2$Ph), 7.2–7.7 (m, 20H, 4Ph); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.6, 27.3, 27.7, 38.1, 64.4, 68.7, 71.5, 72.2, 73.8, 74.6, 81.8, 127.59, 127.64, 128.0, 128.1, 128.2, 128.4, 128.5, 129.0, 129.96, 130.02, 134.0, 135.9, 138.4, 139.6; MS (FAB) *m*/*z* 596 ($M^+$+1), 619 ($M^+$+Na);

HRMS (FAB) *m*/*z* calcd for $C_{37}H_{44}O_5SiNa$ 619.2856 found 619.2852 ($M^+$+Na).

### 4.39. 1,2-Anhydro-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-galactopyranose, D-30

To a solution of D-**28** (50 mg, 88.8 μmol) in $CH_2Cl_2$ (2 ml) at 0 °C was added *m*-CPBA (50–60%, 39.9 mg, 0.116 mmol). After stirring for 22 h at rt, the reaction mixture was quenched with aq $Na_2SO_3$ (22 mg) and the resulting mixture stirred for 30 min. The reaction mixture was extractively worked up with EtOAc and chromatographed on silica gel to give D-**30** (27.9 mg, 54.2%) and D-**26** (21.5 mg, 41.8%) as colorless oils. D-**30**: $[\alpha]_D^{20} = -16.4$ (*c* 1.03, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.07 (s, 9H, –C($CH_3$)$_3$), 1.59–1.9 (m, 3H, H-5, H-5a$_{ax}$, H-5a$_{eq}$), 3.31 (dd, $J = 3.7$, 1.4 Hz, 1H, H-1 or H-2), 3.34 (br d, $J = 3.6$ Hz, 1H, H-2 or H-1), 3.51 (dd, $J = 9.5$, 5.2 Hz, 1H, H-6$_\alpha$), 3.60 (d, $J = 3.1$ Hz, 1H, H-3), 3.68 (t, $J = 9.5$ Hz, 1H, H-6$_\beta$), 4.08 (br s, 1H, H-4), 4.54–5.06 (m, 4H, 2 × –OC$H_2$Ph), 7.27–7.65 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.6, 23.0, 27.2, 36.0, 54.0, 54.4, 64.6, 71.8, 73.3, 75.0, 78.7, 127.6, 127.7, 127.8, 128.0, 128.5, 128.8, 129.98, 130.01, 133.9, 135.9, 138.6, 139.8; MS (FAB) *m*/*z* 579 ($M^+$+1), 601 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{37}H_{42}O_4SiNa$ 601.2750 found 601.2751 ($M^+$+Na).

### 4.40. 1-*O*-Allyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-β-D-galactopyranose, D-31 and 2-*O*-allyl-3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldiphenyl)silyl-5a-carba-α-D-talopyranose, D-27b

To a solution of D-**30** (19.6 mg, 33.9 μmol) in allyl alcohol (1.5 ml) at rt was added TSA (1.7 mg, 8.94 μmol). After stirring for 10 h at 40 °C, $Et_3N$ (two drops) was added and the resulting mixture concentrated by co-evaporation with EtOAc. The residue was filtered on silica gel pad and the filtrate was concentrated and chromatographed on silica gel column to give D-**31** (11.6 mg, 53.8%) and D-**27b** (4.9 mg, 22.7%) as colorless oils. D-**31**: $[\alpha]_D^{21} = -1.4$ (*c* 0.58, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.08 (s, 9H, –C($CH_3$)$_3$), 1.42 (app q, $J = 11.6$ Hz, 1H, H-5a$_{ax}$), 1.57–1.70 (m, 2H, H-5, H-5a$_{eq}$), 3.25 (m, 1H, H-1), 3.28 (dd, $J = 9.7$, 2.1 Hz, 1H, H-3), 3.53 (dd, $J = 9.8$, 5.5 Hz, 1H, H-6$_\alpha$), 3.7 (app t, $J = 9.4$ Hz, 1H, H-6$_\beta$), 4.06–4.16 (m, 3H, H-2, –OC$H_2$CH=CH$_2$), 4.18 (br s, 1H, H-4), 4.55–5.05 (m, 4H, 2 × –OC$H_2$Ph), 5.16 (pseudo dq, $J = 10.3$, 1.5 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.27 (pseudo dq, $J = 17.2$, 1.6 Hz, 1H, –OCH$_2$CH=CH$_\alpha H_\beta$), 5.93 (m, 1H, –OCH$_2$C$H$=CH$_2$), 7.2–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.9, 27.1, 27.6, 40.5, 64.8, 71.2, 73.1, 74.3, 74.9, 75.0, 80.5, 84.5, 117.5, 127.8, 128.0, 128.42, 128.46, 128.48, 128.8, 129.2, 130.38, 133.42, 134.2, 134.3, 135.9, 136.2, 139.1, 140.0; MS (FAB) *m*/*z* 637 ($M^+$+1), 659 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{40}H_{48}O_5SiNa$ 659.3169 found 659.3166 ($M^+$+Na). D-**27b**: $[\alpha]_D^{21} = +35.9$ (*c* 0.24, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.05 (s, 9H, –C($CH_3$)$_3$), 1.27 (m, 1H, H-5a$_{ax}$), 2.45–2.55 (m, 2H, H-5, H-5a$_{eq}$), 3.04 (dd, $J = 9.0$, 2.6 Hz, 1H, H-2), 3.52 (dd, $J = 5.2$, 2.1 Hz, 1H, H-4), 3.8–4.2 (m, 6H, H-1, H-3, H-6$_\alpha$, H-6$_\beta$, –OC$H_2$CH=CH$_2$), 4.33–4.71 (m, 4H, 2 × –OC$H_2$Ph), 5.18 (pseudo dq, $J = 10.3$, 1.3 Hz, 1H, –OCH$_2$CH=C$H_\alpha$H$_\beta$), 5.26 (pseudo dq, $J = 17.2$, 1.5 Hz, –OCH$_2$CH=CH$_\alpha H_\beta$), 5.90 (m, 1H, –OCH$_2$C$H$=CH$_2$), 7.2–7.7 (m, 20H, 4Ph); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.0, 27.7, 29.9, 40.5, 62.7, 66.6, 71.0, 71.4, 74.5, 76.2, 80.0, 83.7, 117.9, 127.9, 128.1, 128.2, 128.3, 128.4, 128.8, 129.0, 130.1, 135.0, 135.3, 136.27, 136.34, 139.2, 139.5; MS (FAB) *m*/*z* 637 ($M^+$+1), 659 ($M^+$+Na); HRMS (FAB) *m*/*z* calcd for $C_{40}H_{48}O_5SiNa$ 659.3169 found 659.3170 ($M^+$+Na).

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