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PAPER

Synthesis of β-*C*-galactosyl D- and L-alanines†‡

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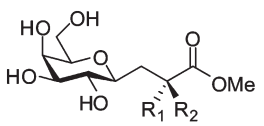
Synthesis of β-*C*-D-galactosyl D- and L-alanines is carried out *via* a highly stereoselective Grignard reaction of glycosyl iodides, Sharpless dihydroxylation and S_N2 displacement of the corresponding mesylate or tosylate. Alternatively, attempted triflation of the intermediate alcohols triggers a stereoselective debenzylative cyclization leading to interesting bicyclic *trans*-fused compounds.

Introduction

Cell surface carbohydrates in the form of glycoconjugates play important roles in various life processes.[1,2] Glycoproteins present key components of cellular recognition processes, signaling pathways and the immune response. Over the past few years, small glycopeptides have been emerging as valuable vaccine candidates and therapeutics.[3–6] One of the factors that limits the utility of glycopeptides as drugs is their chemical and enzymatic instability under physiological conditions. Incorporation of *C*-glycosyl amino acids in such glycopeptides could provide stable glycopeptide analogs which are resistant to cleavage by *O* or *N*-glycosidases as well as acidic hydrolysis.[7–11]

In native glycoproteins, the sugar is linked to the protein either through the OH group of L-serine or L-threonine (*O*-glycoproteins) or through the NH_2 group of L-asparagine (*N*-glycoproteins). Consequently, most of the efforts in this area have been focused on devising syntheses of *C*-glycosyl analogs of serine/threonine and asparagine.[10] In order to access *C*-glycopeptide mimics wherein the sugar is closer to the peptide backbone, we were interested in the synthesis of the chain-shortened *C*-glycosyl alanines **1** (Fig. 1).



1a. R_1 = H, R_2 = NHBoc
1b. R_1 = NHBoc, R_2 = H

Fig. 1 Structures of β-*C*-D-galactopyranosyl alanines.

A few syntheses of *C*-glycosylated alanines have been reported using a variety of methods. The majority of the synthesized *C*-glycosylated amino acids are α-linked pyranosides. For example, Kessler and co-workers[12] employed Bu_3SnH promoted free radical coupling of per-acetylated glycosyl bromides (D-Glc, D-Gal, D-Lac) and urethane protected dehydroalaninate derivatives to obtain α-linked *C*-glycopyranosyl DL-alanines. Alternatively, reductive ring opening of 1,2-anhydro sugars with titanocene(III) chloride and trapping of the so formed free radical with Boc protected dehydroalaninate derivative led to α-*C*-glucopyranosyl DL-alanines.[13] Yet another free radical coupling method, to access α-linked *C*-glycopyranosyl D-alanine, involves $Bu_3SnH/NaCNBH_3$ promoted coupling of per-acetylated glycosyl iodides (D-Glc, D-Gal) and a chiral methyleneoxazolidinone derived from L-alanine itself.[14] Conversion of the known α-*C*-allyl glucopyranoside into α-*C*-glucopyranosyl D- and L-alanines *via* Sharpless AD reaction and subsequent S_N2 displacement of the secondary sulfonate by azido group is reported.[15] A similar strategy has been employed to access the corresponding β-D-GalNAc analogs starting from 2-nitro substituted β-*C*-allyl D-galactopyranoside.[16] Other methods involve asymmetric Strecker synthesis of α-*C*-glycosyl L-alanines (D-Glc, L-fuc),[17] and a sequential olefin cross-metathesis followed by Hg(II) mediated cyclization[18] to obtain α-D-glucopyranosyl D-alanine. Claisen–Ireland [3,3] sigmatropic rearrangement of *exo*-methylene glycals bearing a C-2 glycine ester has been shown to afford glycosylated DL alanine mixture which was transformed into racemic β-D-glucosamine derivative.[19] Likewise, a Wittig reaction of a 2-deoxy D-galactosyl phosphorane with Garner aldehyde and its concomitant hydrogenation afforded 2-deoxy β-*C*-D-galactosyl D-alanine.[20] Dondoni's proline catalyzed electrophilic α-amination of *C*-glycosyl acetaldehydes[21] gives direct access to various α- and β-linked *C*-glycosyl D- and L-alanines. However, to the best of our knowledge the synthesis of β-*C*-D-galactopyranosyl L-alanine **1a** and its corresponding D-alanine analog **1b** has not been previously disclosed. Herein, we report a short synthesis of β-*C*-D-galactopyranosyl D- and L-alanines **1a** and **1b** using an allyl Grignard reaction of per-*O*-benzyl galactosyl iodides as one of the key steps.

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† Dedicated to Prof. M. S. Wadia on the occasion of his 75th birthday.
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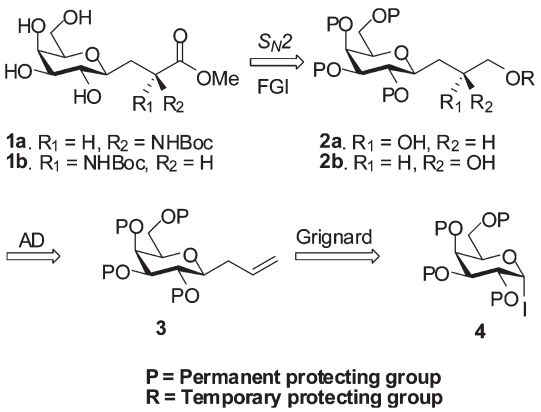
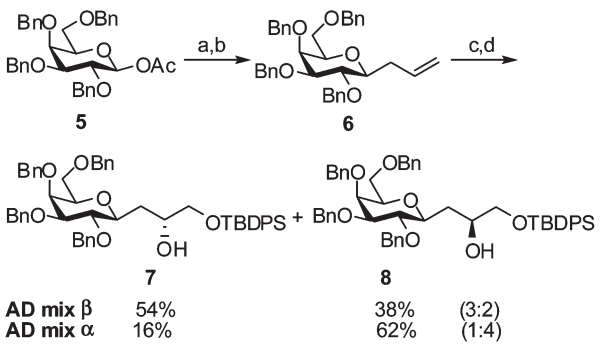
Results and discussion

The retrosynthetic strategy is outlined in Scheme 1. According to previous studies by Gurjar and co-workers, reported in the course of their synthesis of α-D-glucopyranosyl alanines,[15] the target molecule **1a** could be synthesized from secondary alcohol **2a** by nucleophilic displacement of the corresponding sulfonate by azide, followed by functional group inter-conversions. Compound **2a** could be obtained by Sharpless asymmetric dihydroxylation (AD) of the terminal olefin **3** using AD mix-β. It was envisaged that the β-*C*-glycoside could be accessed *via* a stereoselective Grignard reaction of galactosyl iodide **4** with allyl magnesium halide. The same sequence of reactions using AD mix-α would give entry to D-alanine analog **1b** through the intermediacy of alcohol **2b**.

The synthesis began with preparation of the key β-*C*-galactopyranoside **6**. As shown in Scheme 2, treatment of the known and easily accessible 2,3,4,6-tetra-*O*-benzyl β-D-galactopyranosyl acetate **5**[22] with iodotrimethylsilane in CH_2Cl_2 at 0 °C cleanly furnished the corresponding α-iodide. The reaction was completed in 1 h and the formed TMSOAc side product was evaporated by repeated benzene azeotrope. The crude iodide was treated with a 2 M THF solution of allyl magnesium chloride at 0 °C under neat conditions. To our delight, the reaction cleanly generated a single product as judged by TLC. Column chromatography of the crude product afforded the desired β-*C*-allyl compound **6** (85% over two steps) as a single isomer. No α-isomer was encountered, suggesting that the reaction follows a S_N2-type pathway. Formation of a single isomer avoided tedious column chromatography to separate the α/β isomers. Compound **6** has been earlier prepared by Kishi and co-workers using a stereoselective Grignard addition to 2,3,4,6-tetra-*O*-benzyl galactopyrano-lactone followed by triethylsilane reduction of the formed hemiketal in the presence of $BF_3{\cdot}OEt_2$ (76%, α : β = 1 : 10).[23] Arya and co-workers utilized a Grignard reaction of *in situ* generated 2,3,4,6-tetra-*O*-benzyl galactosyl chloride from the corresponding hemiacetal to obtain **6** in 48% yield.[7] More recently, Miller and Gardiner employed direct allylation of methyl glycosides using an allylTMS, TMSOTf, MeCN combination to obtain **6** in 57% yield and in a 1 : 9 α : β ratio.[24] The characterization data for compound **6** matched the reported data[7] and the stereochemistry of **6** was independently confirmed by NOESY analysis.



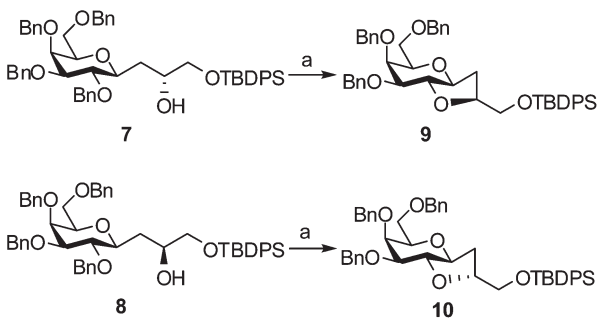
Scheme 1 Retrosynthetic strategy.



Scheme 2 Stereoselective preparation of β-*C*-allyl glycoside **6** and its Sharpless AD reaction. *Reagents and conditions*: (a) TMSI (1.1 equiv), CH_2Cl_2, 0 °C, 1 h; (b) 2.0 M allylmagnesium chloride in THF (3 equiv), 0 °C to rt, 2 h, 85% over two steps; (c) AD mix-α or AD mix-β, *t*-BuOH : H_2O (1 : 1), cat. $K_2OsO_4{\cdot}2H_2O$, 0 °C, 3 d; (d) TBDPSCl (2 equiv), pyridine (13 equiv), rt, 1 d.

Sharpless AD reaction of **6** using AD mix-β furnished a non-separable diastereomeric mixture, which, upon selective TBDPS protection of the primary alcohol,[25] could be readily separated by silica gel column chromatography, to obtain alcohols **7** and **8** in 54% and 38% yields, respectively. The stereochemistry of the faster running major isomer **7** was tentatively assigned as *R* at this stage using Sharpless's mnemonic.[26] In order to confirm the assignment, another reaction was conducted on olefin **6** with AD mix-α. As expected, this reaction afforded **7** as a minor isomer and the slower running **8** as a major isomer in a ratio of 1 : 4. Thus the stereochemistry of **7** and **8** was assigned as **7** (*R*) and **8** (*S*). This exercise also provided access to both diastereomeric alcohols in acceptable yields.

In order to synthesize the L-alanine derivative, alcohol **7** was subjected to triflation using Tf_2O and pyridine in CH_2Cl_2 (Scheme 3). The reaction was completed in 15 min, however, ^1H and ^{13}C NMR analysis of the product indicated peaks corresponding to only 3 benzyl groups along with loss of the OTf group. Further the H-2 proton moved downfield indicating that the 2-OBn group might have been cleaved. MS data showed *m*/*z* peak at 729 corresponding to (M + 1) peak of the debenzylated product. Detailed NMR analysis (see ESI‡) revealed a *trans*-fused bicyclic structure **9**. ^1H–^1H COSY analysis allowed



Scheme 3 Triflation leading to serendipitous debenzylative cycloetherification. *Reagents and conditions*: (a) pyridine (6 equiv), Tf_2O (2 equiv), CH_2Cl_2, 0 °C, 15 min, 57% for **9** and 76% for **10**.

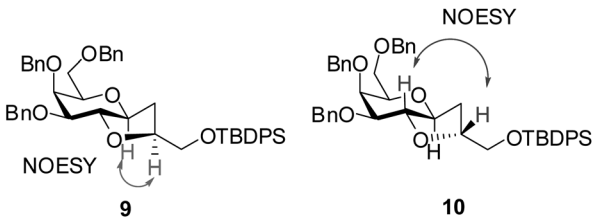
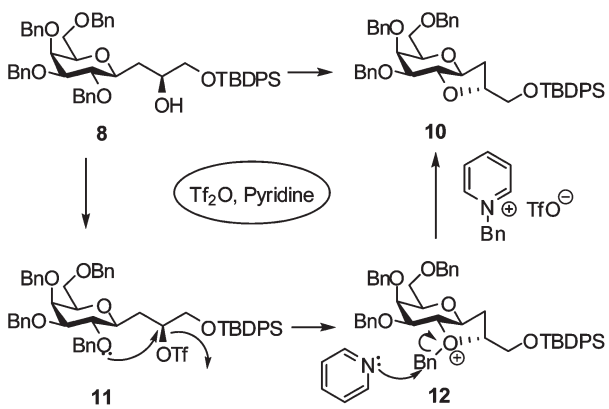


Fig. 2 Key NOESY correlations in **9** and **10**.

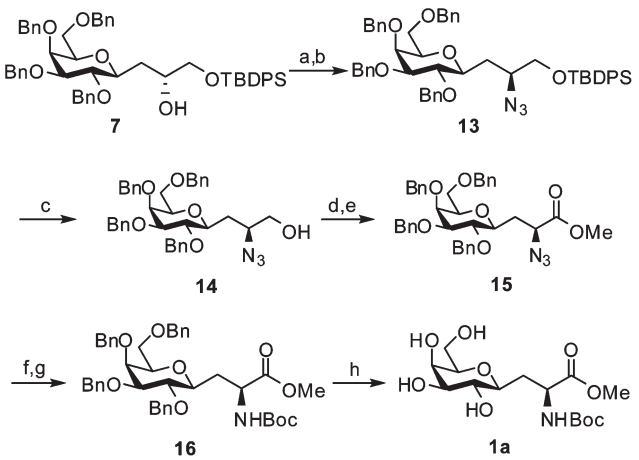
assignment of the H1–H6 sugar and side chain protons. A NOESY spectrum of **9** clearly showed correlation between the proton at the newly formed stereocenter and the anomeric proton H1 (and no correlation with the H2 proton) unambiguously confirming the absolute stereochemistry of the bicyclic structure (Fig. 2). Likewise, triflation of the other isomer **8** under identical conditions afforded the corresponding bicyclic product **10**. NOESY analysis showed a correlation between the proton of the newly formed stereocenter and the H2 ring proton (and no correlation with the H1 proton) confirming the absolute structure of the diastereomer **10**.

Formation of bicyclic compounds **9** and **10** presumably occurred *via* neighboring group participation by the benzyl group during intramolecular displacement of triflate anion, for example in **11**, forming a benzyloxonium ion **12**, which probably undergoes attack by a nucleophile, perhaps pyridine, to release the latent benzylic carbocation (Scheme 4).[27] Such cyclizations are well precedented in the literature and are commonly encountered when the reacting groups are in a 1,4 relationship.[27–32] Similar debenzylative cycloetherifications have been observed in epoxides[33] and allylic systems,[34,35] and in iodoetherification[36,37] reactions. The *trans*-fused bicyclic compounds **9** and **10** could serve as valuable intermediates in the synthesis of the Ezomycin group of antibiotics and related analogs.[38]

Although quite interesting, the cyclization was an obvious obstacle in the planned synthesis of *C*-glycosyl amino acids. After some experimentation, it was realized that, the adventitious cyclization could be circumvented by using tosylates or mesylates in place of triflates (Scheme 5). Thus, tosylation of the *R* alcohol **7** followed by sodium azide nucleophilic displacement afforded the desired azido derivative **13** (65% over two steps) with no trace of the earlier encountered cyclized product **9**.

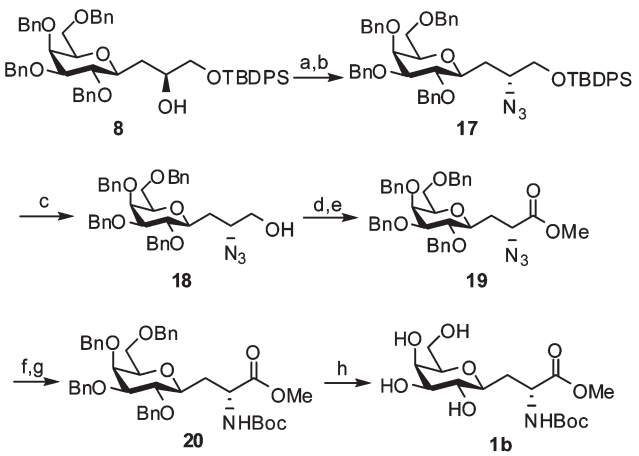


Scheme 4 Proposed mechanism of debenzylative cyclization.



Scheme 5 Synthesis of *C*-β-D-galactosyl-L-alanine **1a**. *Reagents and conditions*: (a) *p*-TsCl (1.5 equiv), pyridine (6 equiv), CH_2Cl_2, 0 °C to 100 °C, 36 h; (b) NaN_3, DMF, 120 °C, 8 h, 65% over two steps; (c) 1 M TBAF in THF, rt, 7 h, 91%; (d) cat. TEMPO, NaBr, 15% $NaHCO_3$, trichloroisocyanuric acid, acetone, 0 °C, 1 h; (e) $SOCl_2$, MeOH, 0 °C to rt, 90 min, 78% over two steps; (f) PPh_3, THF, H_2O, 80 °C, 20 min; (g) Boc_2O (3.5 equiv), Et_3N, CH_2Cl_2, 10 h, 90% over two steps; (h) 20% $Pd(OH)_2$, H_2 (1 atm), MeOH : CH_2Cl_2 (4 : 1), 8 h, 84%.

Removal of the TBDPS group using TBAF revealed the primary alcohol **14** (91%), which upon TEMPO oxidation[39] and concomitant esterification using $SOCl_2$ in MeOH[40] delivered the azido ester **15** (78%, 2 steps). Rapid reduction of the azide to an amino group under modified Staudinger conditions (80 °C, 20 min) and subsequent Boc-protection afforded the fully protected amino acid derivative **16** (90% over two steps). Hydrogenolysis catalyzed by Degussa type $Pd(OH)_2$ reagent[41] using a hydrogen balloon cleanly furnished the desired β-*C*-D-galactosyl-L-alanine **1a** (84%) in good overall yield.



Scheme 6 Synthesis of *C*-β-D-galactosyl-D-alanine **1b**. *Reagents and conditions*: (a) MsCl (2.2 equiv), pyridine (6 equiv), CH_2Cl_2, 0 °C to rt, 3 h; (b) NaN_3, DMF, 120 °C, 7 h, 74% over two steps; (c) 1 M TBAF in THF, rt, 7 h, 80%; (d) cat. TEMPO, NaBr, 15% $NaHCO_3$, trichloroisocyanuric acid, acetone, 0 °C, 1 h; (e) $SOCl_2$, MeOH, 0 °C to rt, 90 min, 82% over two steps; (f) PPh_3, THF, H_2O, 80 °C, 20 min; (g) Boc_2O (3.5 equiv), Et_3N, CH_2Cl_2, 10 h, 90% over two steps; (h) 20% $Pd(OH)_2$, H_2 (1 atm), MeOH, 3 h, 85%.

The D-alanine analog **1b** was prepared under more or less identical conditions. Although tosylation of **8** required reflux conditions and afforded the corresponding chloride (perhaps *via* concomitant S_N2 displacement of the *in situ* generated tosylate), no conversion was observed at RT. Advantageously, mesylation of *S* alcohol **8** cleanly delivered the corresponding mesylate and subsequent S_N2 displacement by azide afforded **17**, which was transformed to **1b** in a similar manner in good overall yield *via* the intermediacy of **18–20** (Scheme 6).

Conclusion

In conclusion, we have carried out the first synthesis of β-*C*-D-galactosyl D- and L-alanines *via* a highly stereoselective Grignard reaction of glycosyl iodides, Sharpless AD and S_N2 displacement of mesylate or tosylate. Glycosyl iodide[42] mediated Grignard reaction allowed direct access to the key β-*C*-glycoside **6** in a highly stereoselective fashion. This protocol could be employed for the synthesis of other sugar analogs of alanines. During our explorations, we also encountered a stereoselective debenzylative cyclization leading to interesting *trans*-fused bicyclic compounds with potential application in natural product synthesis.

Experimental section

General methods

All reactions were conducted under a dry nitrogen atmosphere. Solvents (CH_2Cl_2 >99%, THF 99.5%, Acetonitrile 99.8%, DMF 99.5%) were purchased in capped bottles and dried under sodium or CaH_2. All other solvents and reagents were used without further purification. All glasswares used were oven dried before use. TLC was performed on pre-coated aluminium plates of silica gel 60 F254 (0.25 mm, E. Merck). Developed TLC plates were visualized under a short-wave UV lamp and by heating plates that were dipped in ammonium molybdate/cerium(IV) sulfate solution. Silica gel column chromatography was performed using silica gel (100–200 mesh) and employed a solvent polarity correlated with TLC mobility. NMR experiments were conducted on 400 MHz instrument using $CDCl_3$ (D, 99.8%) or CD_3OD (D, 99.9%) or $(CD_3)_2SO$ (D, 99.9%) as solvents. Chemical shifts are relative to the deuterated solvent peaks and are in parts per million (ppm). ^1H–^1H COSY was used to confirm proton assignments. High resolution mass spectra were acquired under ESI mode using Q-TOF analyzer. Melting points were determined by capillary apparatus. Specific rotation experiments were measured at 589 nm (Na) and 25 °C. IR spectra were recorded on an FT-IR spectrometer using CsCl plates.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-2-propene (6). TMSI (61.3 μL, 0.43 mmol) was added dropwise to a stirred solution of **5** (209 mg, 0.36 mmol) in anhydrous CH_2Cl_2 (3.5 mL) at 0 °C. After 1 h, dry benzene (5 mL) was added at 0 °C and the solvent was evaporated on a rotary evaporator under N_2 atmosphere; azeotroping was repeated twice. To the crude yellowish compound, a solution of allylmagnesium chloride (2.0 M in THF, 0.54 mL) was added dropwise at 0 °C and the reaction was stirred at rt for 2 h. It was quenched by adding ethyl acetate (5 mL) and saturated aq. NH_4Cl (5 mL). The aqueous layer was extracted using ethyl acetate (30 mL × 2) and the combined organic layer was washed with saturated aq. $Na_2S_2O_3$ (15 × 2 mL) and brine (15 × 2 mL), dried over anhydrous Na_2SO_4, concentrated, and dried under vacuum to obtain an oily residue, which was purified by silica gel column chromatography (6% ethyl acetate/pet ether) to afford **6** as a viscous liquid (172 mg, 85% over two steps): $[\alpha]_D^{25}$ +8.8 (*c* 1.31, $CHCl_3$); IR ($CHCl_3$) *ν* 3066, 3032, 1642, 1028, 911 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.5–7.1 (m, 20H, ArH), 5.97–5.87 (m, 1H, Allylic CH), 5.09 (dd, *J* = 1.5, 17.3 Hz, 1H, Allylic CH_2), 5.03 (d, *J* = 10.3 Hz, 1H, Allylic CH_2), 4.94 (d, *J* = 10.7 Hz, 1H, $PhCH_2$), 4.93 (d, *J* = 12.4 Hz, 1H, $PhCH_2$), 4.73, 4.66 (ABq, *J* = 11.7 Hz, 2H, $PhCH_2$), 4.64 (d, *J* = 10.7 Hz, 1H, $PhCH_2$), 4.63 (d, *J* = 12.4 Hz, 1H, $PhCH_2$), 4.46, 4.40 (ABq, *J* = 11.8 Hz, 2H, $PhCH_2$), 3.98 (d, *J* = 2.5 Hz, 1H, H-4), 3.72 (t, *J* = 9.3 Hz, 1H, H-2), 3.59 (dd, *J* = 2.5, 9.3 Hz, 1H, H-3), 3.56–3.50 (m, 3H, H-5, H-6 and H-6′), 3.31 (ddd, *J* = 2.9, 8.5, 9.3 Hz, 1H, H-1), 2.63–2.58 (m, 1H, CHa), 2.32 (ddd, *J* = 4.9, 8.5, 14.4 Hz, 1H, CHb); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.9, 138.6, 138.5, 138.1, 135.3, 128.54, 128.51, 128.3, 128.22, 128.18, 128.0, 127.84, 127.80, 127.74, 127.65, 116.8, 84.1, 79.5, 78.7, 76.9, 75.5, 74.5, 73.8, 73.6, 72.3, 69.1, 36.3; HRMS calcd for $C_{37}H_{41}O_5$ $[M + H]^+$ 565.2954, found 565.2942.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-(2*R*)-ol-3-*tert*-butyl-diphenylsilyloxy-propane (7). A solution of AD mix-β (1.5 g) in 1 : 1 *tert*-butyl alcohol and water (6 mL) was added to a stirred solution of **6** (610 mg, 1.07 mmol) in 1 : 1 *tert*-butyl alcohol and water (4 mL) at 0 °C. Potassium osmate dihydrate (7.2 mg, 0.02 mmol) was added and the reaction was stirred at 0 °C for 3 d. The reaction was stopped by adding sodium sulfite (1.6 g) and kept at rt for 20 min. It was diluted with CH_2Cl_2 (40 mL), washed with water (10 mL) and brine (5 mL), dried over anhydrous Na_2SO_4. The combined organic layer was concentrated on rotary evaporator. To this crude product, pyridine (951 μL, 11.81 mmol) and TBDPSCl (471 μL, 1.82 mmol) were sequentially added and stirred at rt for 1 d, concentrated on a rotary evaporator and co-evaporated with toluene several times. The residue was dissolved in $CHCl_3$ (50 mL), washed with water (10 mL) and dried over anhydrous Na_2SO_4. The chloroform layer was concentrated to get a residue which upon column chromatographic purification on silica gel (11% ethyl acetate/pet ether) afforded (2*R*)-alcohol **7** as a viscous liquid (486 mg, 54% over two steps) and (2*S*)-alcohol **8** (343 mg, 38% over two steps): Compound **7** $[\alpha]_D^{25}$ +5.0 (*c* 1.14, $CHCl_3$); IR ($CHCl_3$) *ν* 3497, 3019, 1219, 1107 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.72–7.63 (m, 4H, ArH), 7.41–7.23 (m, 26H, ArH), 4.93 (d, *J* = 11.3 Hz, 2H, $PhCH_2$), 4.74, 4.68 (ABq, *J* = 11.7 Hz, 2H, $PhCH_2$), 4.66 (d, *J* = 10.6 Hz, 1H, $PhCH_2$), 4.60 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.42, 4.37 (ABq, *J* = 11.8 Hz, 2H, $PhCH_2$), 3.97–3.93 (m, 2H, H-4 and C*H*OH), 3.72 (t, *J* = 9.3 Hz, 1H, H-2), 3.64 (dd, *J* = 5.5, 10.0 Hz, 1H, $CH_2O(CH_3)_3CSi$), 3.62–3.38 (m, 7H, H-1, H-3, H-5, H-6a, H-6b, OH and $CH_2O(CH_3)_3CSi$), 2.32–2.29 (m, 1H, CHa), 1.65 (dt, *J* = 5.0, 9.4 Hz, 1H, CHb), 1.03 (s, 9H, $(CH_3)_3CSi$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.6, 138.34, 138.25, 137.8, 135.70, 135.68, 133.6, 133.5, 129.8, 128.58, 128.56, 128.50, 128.4, 128.3, 128.2, 128.1, 127.9, 127.82, 127.79, 127.7, 84.5, 80.0, 78.9, 76.9, 75.7, 74.6, 73.7, 72.4, 71.9, 69.0, 67.7, 35.2,

27.0, 19.3; HRMS calcd for $C_{53}H_{60}O_7SiNa$ $[M + Na]^+$ 859.4006, found 859.3976.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl-(2*S*)-ol-3-*tert*-butyl-diphenylsilyloxy-propane (8). The same procedure as described above was followed for AD reaction of alkene **6** (343 mg, 0.61 mmol) using AD mix-α (0.85 g) to afford **8** (314 mg, 62% over two steps) and **7** (76 mg, 16% over two steps). Compound **8** $[\alpha]_D^{25}$ −0.3 (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) *ν* 3242, 3015, 1217, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.65–7.62 (m, 4H, ArH), 7.43–7.23 (m, 26H, ArH), 4.93 (d, *J* = 11.0 Hz, 1H, $PhCH_2$), 4.92 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.74, 4.66 (ABq, *J* = 12.5 Hz, 2H, $PhCH_2$), 4.63 (d, *J* = 13.3 Hz, 2H, $PhCH_2$), 4.41, 4.38 (ABq, *J* = 11.8 Hz, 2H, $PhCH_2$), 3.98 (d, *J* = 2.3 Hz, 1H, H-4), 3.98–3.97 (m, 1H, C*H*OH), 3.69–3.58 (m, 3H), 3.56–3.46 (m, 5H), 2.73 (br s, 1H, OH), 2.06 (ddd, *J* = 2.2, 9.2, 14.3 Hz, 1H, CHa), 1.56 (ddd, *J* = 3.0, 9.8, 14.3 Hz, 1H, CHb), 1.03 (s, 9H, $(CH_3)_3CSi$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.9, 138.4, 138.0, 137.8, 135.7, 133.4, 129.9, 128.6, 128.5, 128.40, 128.36, 128.2, 128.0, 127.92, 127.87, 127.76, 127.73, 127.69, 84.9, 78.8, 77.5, 76.9, 76.8, 75.5, 74.6, 73.6, 72.4, 68.9, 68.8, 68.2, 35.1, 27.0, 19.4; HRMS calcd for $C_{53}H_{60}O_7SiNa$ $[M + Na]^+$ 859.4006, found 859.3994.

Bi-cyclic compound (9). To a stirred solution of **7** (132 mg, 0.16 mmol) in CH_2Cl_2 (2.0 mL) and pyridine (80 μL, 0.95 mmol), was added trifluoromethanesulfonic anhydride (53 μL, 0.32 mmol) in a slow dropwise manner at 0 °C, over a period of 15 min. After the addition was over, the reaction mixture was diluted with CH_2Cl_2 and successively washed with aq. $NaHCO_3$ (15 mL), water (15 mL) and brine (15 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated on a rotary evaporator and the crude product was purified by column chromatography on silica gel (10% ethyl acetate/pet ether) to obtain compound **9** as a viscous liquid (65 mg, 57%): $[\alpha]_D^{25}$ −4.4 (*c* 0.95, $CHCl_3$); IR ($CHCl_3$) *ν* 2930, 1471, 1382, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.74–7.72 (m, 4H, ArH), 7.40–7.26 (m, 21H, ArH), 4.99 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.97 (d, *J* = 12.5 Hz, 1H, $PhCH_2$), 4.72 (d, *J* = 12.2 Hz, 1H, $PhCH_2$) 4.60 (d, *J* = 11.3 Hz, 1H, $PhCH_2$), 4.53, 4.43 (ABq, *J* = 11.9 Hz, 2H, $PhCH_2$) 4.37–4.30 (m, 1H, C*H*$CH_2O(CH_3)_3CSi$), 4.03 (t, *J* = 9.3 Hz, 1H, H-2), 3.95 (s, 1H, H-4), 3.77–3.62 (m, 5H, H-3, H-5, H-6a and $CH_2O(CH_3)_3CSi$), 3.54 (dd, *J* = 6.0, 9.0 Hz, 1H, H-6b), 3.40–3.34 (m, 1H, H-1), 2.27 (dt, *J* = 6.9, 11.2 Hz, 1H, CHa), 1.89 (app. q, *J* = 8.9, 11.0 Hz, 1H, CHb), 1.06 (s, 9H, $(CH_3)_3CSi$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.9, 138.6, 137.8, 135.7, 135.6, 133.5, 133.4, 129.6, 128.4, 128.1, 127.9, 127.7, 127.4, 127.3, 82.4, 80.2, 79.7, 78.0, 76.7, 75.4, 75.2, 73.5, 72.0, 69.1, 66.3, 31.0, 19.2; HRMS calcd for $C_{46}H_{53}O_6Si$ $[M + H]^+$ 729.3611, found 729.3587.

Bi-cyclic compound (10). The same procedure as described earlier for triflation of **7** was used for alcohol **8** (209 mg, 0.25 mmol) to obtain **10** (138 mg, 76% over two steps) as a white solid: $[\alpha]_D^{25}$ −9.8 (*c* 1.53, $CHCl_3$); mp 112–113 °C; IR ($CHCl_3$) *ν* 3069, 3032, 1472, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.77–7.72 (m, 4H, ArH), 7.46–7.26 (m, 21H, ArH), 5.00 (d, *J* = 11.0 Hz, 1H, $PhCH_2$), 4.98 (d, *J* = 12.2 Hz, 1H, $PhCH_2$), 4.73 (d, *J* = 12.2 Hz, 1H, $PhCH_2$) 4.61 (d, *J* = 11.0 Hz, 1H, $PhCH_2$), 4.54, 4.46 (ABq, *J* = 11.9 Hz, 2H, $PhCH_2$) 4.36–4.32 (m, 1H, C*H*$CH_2O(CH_3)_3CSi$), 3.99 (t, *J* = 9.3 Hz, 1H, H-2), 3.97 (s, 1H, H-4), 3.80 (dd, *J* = 3.5, 11.0 Hz, 1H, $CH_2O(CH_3)_3CSi$), 3.72–3.66 (m, 4H, H-3, H-5, H-6a and $CH_2O(CH_3)_3CSi$), 3.58 (dd, 1H, H-6b), 3.47 (app. q, *J* = 8.8, 9.1, 9.3 Hz, 1H, H-1), 3.56–3.44 (m, 1H, CHa), 1.89 (app. q, *J* = 10.5 Hz, 1H, CHb), 1.08 (s, 9H, $(CH_3)_3CSi$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.9, 138.7, 138.0, 135.9, 135.73, 135.68, 133.70, 133.6, 129.9, 129.8, 128.58, 128.56, 128.5, 128.3, 128.1, 127.94, 127.86, 127.82, 127.7, 127.6, 82.6, 80.4, 80.3, 79.5, 78.5, 75.5, 73.7, 72.3, 69.2, 66.2, 30.8, 27.0, 19.5; HRMS calcd for $C_{46}H_{53}O_6Si$ $[M + H]^+$ 729.3611, found 729.3593.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-(2*S*)-azido-3-*tert*-butyl-diphenylsilyloxy-propane (13). To a stirred solution of **7** (323 mg, 0.39 mmol) in CH_2Cl_2 (3.4 mL) was successively added pyridine (0.47 mL, 5.78 mmol) and *p*-TsCl (111 mg, 0.58 mmol) at 0 °C and the reaction was refluxed (100 °C) for 36 h. It was quenched by adding aq. NH_4Cl (5 mL) and extracted with EtOAc (30 mL), washed with H_2O (10 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated on a rotary evaporator and the obtained residue was purified using column chromatography on silica gel (10% ethyl acetate/pet ether) to afford the corresponding tosylate. It was dissolved in DMF (3.3 mL), NaN_3 (46 mg, 0.694 mmol) was added and stirred for 8 h at 120 °C. Reaction mixture was diluted with $CHCl_3$ (30 mL), washed with H_2O (10 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated and column chromatographic purification of the residue on silica gel (7% ethyl acetate/pet ether) gave compound **13** as a viscous liquid (216 mg, 65% over two steps): $[\alpha]_D^{25}$ −7.0 (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) *ν* 3032, 2931, 2111, 1261 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.68–7.64 (m, 4H, ArH), 7.44–7.22 (m, 26H, ArH), 4.92 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.91 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.73 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.66 (d, *J* = 9.3 Hz, 1H, $PhCH_2$), 4.63 (d, *J* = 9.3 Hz, 1H, $PhCH_2$), 4.59 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.44, 4.42 (ABq, *J* = 11.7 Hz, 2H, $PhCH_2$), 4.0 (s, 1H, H-4), 3.72 (m, 2H, H-3 and CHN_3), 3.69–3.51 (m, 6H, H-2, H-5, H-6a, H-6b, $CH_2O(CH_3)_3CSi$), 3.43 (m, 1H, H-1), 1.98 (m, 1H, CHa), 1.41 (ddd, *J* = 2.3, 11.3, 14.3 Hz, 1H, CHb), 1.05 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.8, 138.43, 138.35, 138.1, 135.8, 135.7, 133.19, 133.17, 129.9, 128.6, 128.5, 128.48, 128.39, 128.2, 128.0, 127.95, 127.91, 127.81, 127.79, 127.7, 84.9, 79.0, 77.5, 76.3, 75.5, 74.7, 73.7, 73.6, 72.5, 68.8, 67.8, 60.4, 33.1, 26.8, 19.3; HRMS calcd for $C_{53}H_{60}N_3O_6Si$ $[M + H]^+$ 862.4251, found 862.4260.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-(2*S*)-azido-3-propanol (14). To a solution of **13** (210 mg, 0.24 mmol) in THF (2.5 mL) was added a solution of 1.0 M TBAF in THF (0.49 mL, 0.49 mmol) at rt and the reaction stirred for 8 h. It was diluted with CH_2Cl_2 (30 mL), washed with H_2O (10 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated and column chromatographic purification of the crude residue on silica gel (30% ethyl acetate/pet ether) yielded compound **14** as a viscous liquid (138 mg, 91%): $[\alpha]_D^{25}$ −2.5 (*c* 0.94, $CHCl_3$); IR ($CHCl_3$) *ν* 3432, 3020, 2105, 1216, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.37–7.20

(m, 20H, ArH), 4.95 (d, J = 11.0 Hz, 1H, $PhCH_2$), 4.92 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.74, 4.67 (ABq, J = 11.8 Hz, 2H, $PhCH_2$), 4.63 (d, J = 11.0 Hz, 1H, $PhCH_2$), 4.62 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.43, 4.42 (ABq, J = 11.8 Hz, 2H, $PhCH_2$), 3.97 (d, J = 2.3 Hz, 1H, H-4), 3.68–3.52 (m, 6H, H-2, H-3, H-5, H-6a, H-6b and CHN_3), 3.49–3.45 (m, 2H, $CH_2O(CH_3)_3CSi$), 3.39 (m, 1H, H-1), 2.36 (br s, 1H, OH), 2.02 (m, 1H, CHa), 1.71 (ddd, J = 4.8, 9.6, 14.0 Hz, 1H, CHb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.3, 138.2, 137.9, 128.6, 128.55, 128.45, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 84.8, 78.7, 77.5, 76.6, 75.5, 74.7, 73.64, 73.60, 72.4, 68.9, 65.5, 61.3, 33.4; HRMS calcd for $C_{37}H_{42}N_3O_6$ $[M + H]^+$ 624.3074, found 624.3057.

Methyl 3C-(β-2,3,4,6-tetra-*O*-benzyl-galactopyranosyl)-(2*S*)-azido propionate (15). To a stirred solution of alcohol **14** (128 mg, 0.21 mmol) in acetone (2.0 mL) was sequentially added 15% $NaHCO_3$ (0.62 mL), NaBr (4.0 mg, 0.04 mmol) and TEMPO (6.4 mg, 0.04 mmol) at 0 °C. Subsequently, trichloroisocyanuric acid (95 mg, 0.4 mmol) was added portion-wise over 5 min and the reaction was allowed to stir at 0 °C for 1 h. Isopropanol (120 μL) was added to it and reaction mixture was filtered through Celite-545, washed with acetone (50 mL), and the solution was concentrated. The white residue was partitioned between EtOAc (30 mL) and H_2O (10 mL) and organic layer was treated with 2.0 M HCl (0.98 mL), washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was taken in dry MeOH (2.2 mL) and $SOCl_2$ was added dropwise (22 μL, 0.31 mmol) at 0 °C over a period of 5 min. It was stirred at 0 °C and gradually allowed to warm up to rt over a period of 90 min. The reaction mixture was concentrated and the residue was dissolved in CH_2Cl_2 (30 mL), washed with $NaHCO_3$ (15 mL), water (15 mL) and brine (15 mL) and dried over anhydrous Na_2SO_4. The organic layer was concentrated and column chromatographic purification of the residue on silica gel (7% ethyl acetate/pet ether) afforded compound **15** as a white solid (104 mg, 78% over two steps): $[\alpha]_D^{25}$ −16.8 (c 0.60, $CHCl_3$); mp 58–59 °C; IR ($CHCl_3$) ν 3016, 2110, 1742, 1215 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 20H, ArH), 4.95 (d, J = 11.0 Hz, 1H, $PhCH_2$), 4.94 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.75, 4.67 (ABq, J = 11.8 Hz, 2H, $PhCH_2$), 4.63 (d, J = 11.6 Hz, 2H, $PhCH_2$), 4.44, 4.43 (ABq, J = 11.7 Hz, 2H, $PhCH_2$), 4.14 (dd, J = 3.2, 11.3 Hz, 1H, CHN_3), 4.01 (d, J = 2.4 Hz, 1H, H-4), 3.73 (s, 3H, CO_2Me), 3.67 (t, J = 9.3 Hz, 1H, H-2), 3.62 (dd, J = 2.4, 9.3 Hz, 1H, H-3), 3.58–3.53 (m, 3H, H-5, H-6a, H-6b), 3.42 (m, 1H, H-1), 2.15 (ddd, J = 2.0, 11.7, 11.9 Hz, 1H, CHa), 1.93 (ddd, J = 3.3, 10.7 Hz, 1H, CHb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 138.6, 138.24, 138.19, 137.9, 128.5, 128.46, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.66, 84.7, 78.5, 76.9, 75.4, 75.3, 74.7, 73.6, 73.5, 72.4, 68.7, 58.6, 52.6, 33.9; HRMS calcd for $C_{38}H_{42}N_3O_7$ $[M + H]^+$ 652.3023, found 652.3022.

Methyl 3C-β-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-*N*-tert-butoxycarbonyl-L-alanine (16). To a stirred solution of **15** (69 mg, 0.11 mmol) in THF (2.4 mL) was added triphenylphosphine (56 mg, 0.21 mmol) and H_2O (10 μL, 0.55 mmol) at rt and the reaction mixture was heated at 80 °C. After 20 min, solvents were evaporated and residue was co-evaporated with toluene several times *in vacuo*. The residue was dissolved in dry CH_2Cl_2 (2.2 mL) and Et_3N (31 μL) and Boc_2O (85 μL, 0.37 mmol) added dropwise and the reaction stirred for 10 h. Reaction mixture was concentrated *in vacuo*, diluted with EtOAc (30 mL), washed with H_2O (10 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated and column chromatographic purification of the residue on silica gel (16% ethyl acetate/pet ether) yielded compound **16** as a white solid (69 mg, 90% over two steps): $[\alpha]_D^{25}$ −0.2 (c 0.33, $CHCl_3$); mp 113–114 °C; IR ($CHCl_3$) ν 3019, 1742, 1712, 1423, 1216 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 20H, ArH), 5.64 (d, J = 8.6 Hz, 1H, NH), 4.93 (d, J = 10.9 Hz, 1H, $PhCH_2$), 4.92 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.73 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.64 (d, J = 11.6 Hz, 1H, $PhCH_2$), 4.61 (d, J = 11.6 Hz, 2H, $PhCH_2$), 4.53–4.50 (m, 2H, $PhCH_2$ and CHCOO), 4.41 (d, J = 11.8 Hz, 1H, $PhCH_2$), 3.95 (s, 1H, H-4), 3.68 (s, 3H, CO_2Me), 3.66 (t, J = 9.2 Hz, 1H, H-2), 3.58–3.47 (m, 4H, H-3, H-5, H-6a, H-6b), 3.29 (t, J = 9.20, 9.28 Hz, 1H, H-1), 2.26 (m, 1H, CHa), 1.91 (ddd, J = 3.6, 10.4 Hz, 12.1 Hz, 1H, CHb), 1.38 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 155.8, 138.6, 138.3, 138.2, 138.0, 128.6, 128.55, 128.4, 128.39, 128.2, 128.1, 128.0, 127.9, 127.86, 127.8, 127.7, 84.8, 79.6, 78.3, 76.9, 75.6, 74.7, 73.6, 72.6, 68.9, 52.3, 51.7, 33.4, 28.4; HRMS calcd for $C_{43}H_{52}NO_9$ $[M + H]^+$ 726.3642, found 726.3616.

Methyl β-D-galactopyranosyl-*N*-*tert*-butoxycarbonyl-L-alanine (1a). To a solution of **16** (83 mg, 0.11 mmol) in anhydrous MeOH–CH_2Cl_2 (4 : 1), was added vacuum dried Degussa type $Pd(OH)_2$/C (70 mg, 20%). It was stirred at rt for 8 h under a hydrogen atmosphere using a H_2 balloon (1 atm). It was filtered through celite-545 and washed with 50% MeOH and $CHCl_3$ solution. The organic layer was concentrated *in vacuo*. Column chromatographic purification of the residue on silica gel (12% MeOH–CH_2Cl_2) afforded compound **1a** as a viscous liquid (35 mg, 84% yield): $[\alpha]_D^{25}$ +4.7 (c 0.58, $CHCl_3$); IR ($CHCl_3$) ν 3406, 3020, 1736, 1700, 1216 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD) δ 4.13–4.09 (m, 1H), 3.90 (s, 1H, H-4), 3.82 (dd, J = 6.8, 11.6 Hz, 1H), 3.75 (s, 3H, CO_2Me), 3.67 (dd, J = 4.4, 11.6 Hz, 1H), 3.45–3.4 (m, 3H), 3.21–3.16 (m, 1H), 2.24–2.17 (m, 1H, CHa), 1.96 (ddd, J = 3.6, 10.8, 14.4 Hz, 1H, CHb), 1.27 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 156.2, 80.3, 78.7, 76.3, 75.2, 71.4, 69.8, 62.0, 52.7, 50.7, 34.1, 28.4; HRMS calcd for $C_{15}H_{28}NO_9$ $[M + H]^+$ 366.1764, found 366.1773.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-(2*R*)-azido-3-*tert*-butyldiphenylsilyloxy propane (17). To a stirred solution of **8** (185 mg, 0.22 mmol) in CH_2Cl_2 (2.2 mL) at 0 °C was sequentially added pyridine (0.11 mL, 1.33 mmol) and MsCl (0.037 mL, 0.486 mmol). The reaction was allowed to warm up to rt over 3 h. It was diluted with CH_2Cl_2 (30 mL), washed with $NaHCO_3$ (15 mL), H_2O (10 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The organic layer was concentrated *in vacuo* and the crude product was purified by column chromatography on silica gel (10% ethyl acetate/pet ether) to afford the corresponding mesylate. This was dissolved in DMF (2.2 mL), NaN_3 (29 mg, 0.442 mmol) was added and the reaction mixture was heated overnight at 120 °C. It was diluted with $CHCl_3$ (30 mL), washed with H_2O (10 mL) and brine (5 mL), and dried

over anhydrous Na_2SO_4. The organic layer was concentrated on a rotary evaporator and the residue was purified by column chromatography on silica gel (7% ethyl acetate/pet ether) to afford compound **17** as a viscous liquid (141 mg, 74% over two steps): $[\alpha]_D^{25}$ +0.8 (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) *ν* 3018, 2960, 2105, 1216, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.74–7.63 (m, 4H, ArH), 7.43–7.21 (m, 26H, ArH), 4.93 (d, *J* = 10.9 Hz, 1H, $PhCH_2$), 4.91 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.73 (d, *J* = 11.8 Hz, 1H, $PhCH_2$), 4.65 (s, 2H, $PhCH_2$), 4.61 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.38, 4.37 (ABq, *J* = 11.8 Hz, 2H, $PhCH_2$), 3.95 (d, *J* = 2.3, 1H, H-4), 3.73 (dd, *J* = 2.3, 10.2 Hz, 1H, H-3), 3.69–3.58 (m, 3H, H-5, H-6a and CHN_3), 3.51–3.46 (m, 2H, H6b and H-2), 3.41 (dd, *J* = 5.3, 9.0 Hz, 1H, $CH_2O(CH_3)_3CSi$), 3.32 (dd, *J* = 5.84, 7.08 Hz, 1H, $CH_2O(CH_3)_3CSi$), 3.12 (td, *J* = 4.0, 9.1 Hz, 1H, H-1), 2.05 (ddd, *J* = 2.9, 7.8, 14.1 Hz, 1H, CHa), 1.67 (ddd, *J* = 5.2, 9.0, 14.1 Hz, 1H, CHb), 1.04 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.8, 138.4, 138.37, 138.0, 135.9, 135.8, 133.3, 133.3, 129.9, 128.6, 128.5, 128.4, 128.3, 128.28, 128.1, 128.05, 128.0, 127.9, 127.85, 127.8, 127.75, 127.7, 127.6, 84.8, 78.8, 77.1, 76.6, 75.5, 74.7, 73.62, 73.55, 72.3, 68.8, 66.4, 60.8, 32.8, 26.9, 19.3. HRMS calcd for $C_{53}H_{60}N_3O_6Si$ $[M + H]^+$ 862.4251, found 862.4238.

1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-(2*R*)-azido-3-propanol (18). The same procedure as described for **14** was followed for de-silylation of compound **17** (180 mg, 0.21 mmol) to afford **18** (104 mg, 80%) as a white solid: $[\alpha]_D^{25}$ −8.9 (*c* 0.96, $CHCl_3$); mp 81.7–82.7 °C; IR ($CHCl_3$) *ν* 3463, 3065, 2106, 1454, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.37–7.21 (m, 20H, ArH), 4.96 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.93 (d, *J* = 12.2 Hz, 1H, $PhCH_2$), 4.74 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.66 (d, *J* = 11.6 Hz, 2H, $PhCH_2$), 4.61 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.43, 4.41 (ABq, *J* = 11.8 Hz, 2H, $PhCH_2$), 3.94 (d, *J* = 2.3 Hz, 1H, H-4), 3.70 (t, *J* = 9.3 Hz, 1H, H-2), 3.66–3.51 (m, 6H, H-3, H-5, H-6a, H-6b, $CH_2O(CH_3)_3CSi$ and CHN_3), 3.41 (m, 2H, $CH_2O(CH_3)_3CSi$ and H-1), 2.59 (br s, 1H, OH), 2.06 (m, 1H, CHa), 1.82 (ddd, *J* = 4.4, 9.0, 14.5 Hz, 1H, CHb); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.5, 138.2, 138.17, 137.8, 128.6, 128.58, 128.4, 128.3, 128.33, 128.1, 128.0, 127.9, 127.8, 127.7, 84.9, 78.1, 77.5, 76.3, 75.5, 74.7, 73.7, 73.6, 72.4, 69.1, 64.1, 60.9, 32.7; HRMS calcd for $C_{37}H_{42}N_3O_6$ $[M + H]^+$ 624.3074, found 624.3068.

Methyl 3C-(β-2,3,4,6-tetra-*O*-benzyl-galactopyranosyl)-(2*S*)-azido propionate (19). The same procedure as described for **15** was followed for oxidation followed by esterification of azido alcohol **18** (90 mg, 0.14 mmol) to afford **19** (79 mg, 82% over two steps) as a viscous liquid: $[\alpha]_D^{25}$ −2.2 (*c* 0.39, $CHCl_3$); IR ($CHCl_3$) *ν* 3019, 2928, 2109, 1745, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.41–7.26 (m, 20H, ArH), 5.0 (d, *J* = 10.6 Hz, 1H, $PhCH_2$), 4.97 (d, *J* = 10.6 Hz, 1H, $PhCH_2$), 4.78 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.70 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.69 (d, *J* = 11.8 Hz, 1H, $PhCH_2$), 4.66 (d, *J* = 11.8 Hz, 1H, $PhCH_2$), 4.46, 4.48 (ABq, *J* = 11.7 Hz, 2H, $PhCH_2$), 4.13 (dd, *J* = 5.3, 7 Hz, 1H, CHN_3), 4.05 (d, *J* = 2.1 Hz, 1H, H-4), 3.76 (m, 4H, CO_2Me and H-5), 3.63 (dd, *J* = 2.2, 9.3 Hz, 1H, H-3), 3.57 (m, 3H, H-2, H-6a and H-6b), 3.42 (m, 1H, H-1), 2.37 (ddd, *J* = 2.8, 7.5, 14 Hz, 1H, CHa), 1.99 (ddd, *J* = 5.1, 9, 14 Hz, 1H, CHb); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.7, 138.8, 138.2, 138.18, 137.9, 128.5, 128.49, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 84.8, 78.2, 75.7, 75.3, 74.7, 73.6, 73.5, 72.2, 68.5, 59.0, 52.5, 33.9; HRMS calcd for $C_{38}H_{42}N_3O_7$ $[M + H]^+$ 652.3023, found 652.3019.

Methyl 3C-β-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine (20). The same procedure as described for **16** was followed for reduction followed by Boc protection of azido ester **19** (79 mg, 0.12 mmol) to afford **20** (79 mg, 90% over two steps) as a viscous liquid: $[\alpha]_D^{25}$ −10.6 (*c* 1.72, $CHCl_3$); IR ($CHCl_3$) *ν* 3020, 1746, 1707, 1498, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.35–7.26 (m, 20H, ArH), 5.42 (d, *J* = 6.3 Hz, 1H, NH), 4.93 (d, *J* = 11.4 Hz, 2H, $PhCH_2$), 4.74 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.66 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.64 (d, *J* = 11.5 Hz, 1H, $PhCH_2$), 4.61 (d, *J* = 11.9 Hz, 1H, $PhCH_2$), 4.43 (m, 3H, $PhCH_2$ and CHCOO), 4.00 (d, *J* = 1.9 Hz, 1H, H-4), 3.67 (t, *J* = 9.7, 18.1 Hz, 1H, H-2), 3.66 (s, 3H, CO_2Me), 3.59 (dd, *J* = 2.0, 9.2 Hz, 1H, H-3), 3.5 (m, 3H, H-5, H-6a and H-6b), 3.36 (app. t, *J* = 9.2 Hz, 1H, H-1), 2.36 (m, 1H, CHa), 1.87 (m, 1H, CHb), 1.40 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 173.1, 155.3, 138.9, 138.4, 138.3, 137.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.86, 127.8, 127.7, 84.8, 79.8, 78.4, 76.7, 76.5, 75.54, 74.7, 73.7, 73.6, 72.3, 68.5, 52.2, 51.6, 34.1, 28.5. HRMS calcd for $C_{43}H_{52}NO_9$ $[M + H]^+$ 726.3642, found 726.3616.

Methyl β-D-galactopyranosyl-*N*-*tert*-butoxycarbonyl-D-alanine (1b). The same procedure as described for **1a** was followed for de-benzylation of **20** (96 mg, 0.13 mmol) in anhydrous methanol (3 mL) to afford **1b** (41 mg, 85%) as a viscous liquid: $[\alpha]_D^{25}$ −24.3 (*c* 0.58, $CHCl_3$); IR ($CHCl_3$) *ν* 3393, 2929, 1767, 1695, 1217 cm^{-1}; ^1H NMR (400 MHz, DMSO) *δ* 7.15 (d, *J* = 7.2 Hz, 1H, NH), 4.80 (d, *J* = 4.8 Hz, 1H), 4.66 (s, 1H), 4.34 (t, *J* = 4.8, 5.2 Hz, 1H), 4.27 (d, *J* = 4.4 Hz, 1H), 4.16 (app. q, *J* = 5.2, 7.2, 7.6 Hz, 1H), 3.66 (s, 1H), 3.58 (s, 3H, CO_2Me), 3.46–3.34 (m, 2H), 3.24–3.14 (m, 3H), 3.09–3.05 (m, 1H), 2.14 (dd, *J* = 8.0, 12.4 Hz, 1H, CHa), 1.66–1.59 (m, 1H, CHb), 1.37 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 174.4, 155.9, 80.5, 78.5, 76.7, 75.2, 71.4, 69.8, 62.2, 52.8, 51.3, 29.9, 28.5; HRMS calcd for $C_{15}H_{28}NO_9$ $[M + H]^+$ 366.1738, found 366.1754.

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