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# Diastereoselective Synthesis of β-(3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine

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*Abstract:* Key steps in the synthesis of β-(3,4,6-tri-*O*-benzyl-2-deoxy-ß-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine are the Wittig reaction of 2-deoxy-galactopyranosylphosphonium salt **2** and Garner aldehyde, as well as the subsequent diastereoselective hydrogenation of the olefinated sugar **3a,b**. 

## Introduction

Glycopeptides are involved in various important biological processes. They play a crucial role in cell surface recognition, interactions with bacteria, viruses as well as tumor cells.[1] Glycosylation is known to affect the properties of a protein in various ways. In e.g. bioavailability, folding, solubility, as well as stability against proteases can be improved.[2] Usually *N*-or *O*-linked glycopeptides are occurring in nature.[3] They often show an inherent lack of in vivo stability under acidic and basic conditions.[4] Here more stable isosteric *C*-glycosylated peptides became of interest. Therefore during the last decade several different synthetic pathways for the synthesis of *C*-glycosylamino acids have been described.[5]

## Results and Discussion

Here we describe the synthesis of a β-D-galactosyl-alanine derivative. In a recent communication we reported on the stereoselective syntheses of olefinated sugars at the anomeric center *via* Wittig reaction of glycosyl phosphonium tetrafluoroborates.[6] As a key step we now applied this methodology for the preparation of β-(3,4,6-tri-*O*-benzyl-2-deoxy-ß-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine. Reaction of methyl 3,4,6-tri-*O*-benzyl-2-deoxy-galactopyranoside[7] (**1**) with hydrogentriphenylphosphonium tetrafluoroborate[8] in acetonitrile for one hour at reflux gave phosphonium salt **2a,b** in quantitative yield and in a α,β-ratio of 1/1 (Scheme 1). The isomers could be separated by crystallization and X-ray analyses of both could be obtained.[9]

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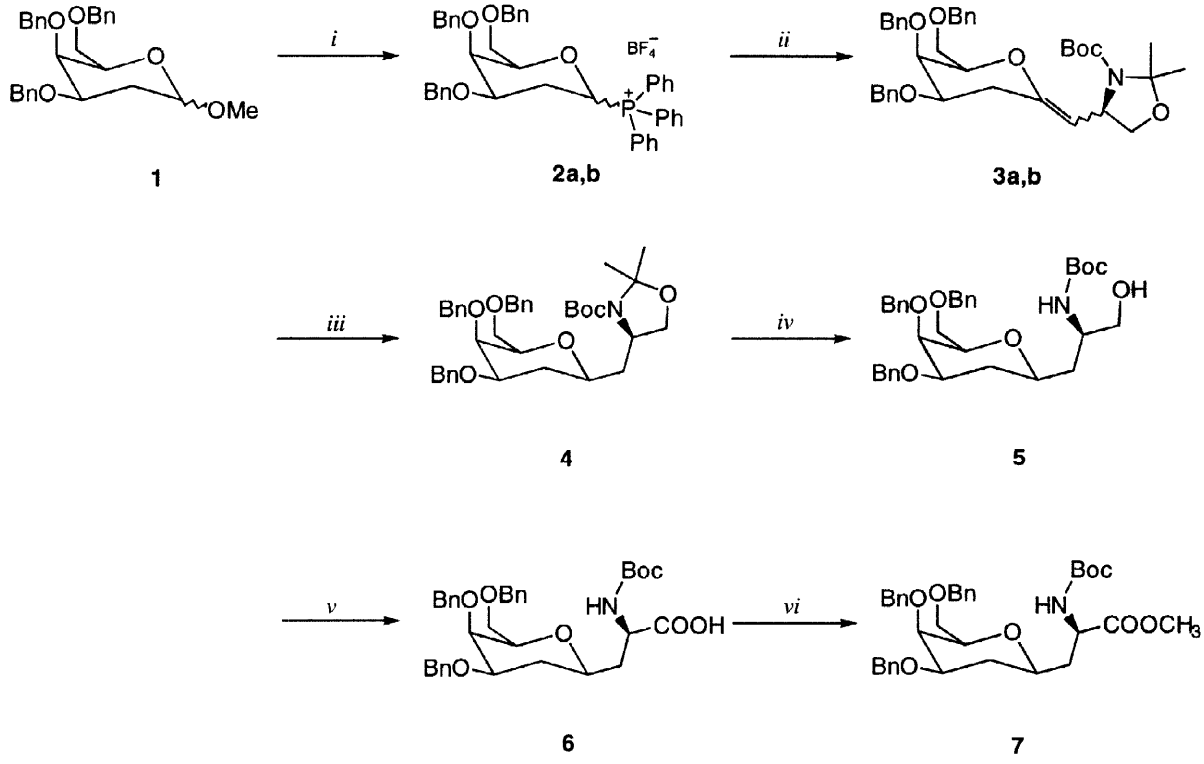
Wittig reaction of the α,β mixture of phosphonium salt **2a,b** and Garner aldehyd[10] using n-BuLi in THF gave the exocyclic enolethers **3a,b**. After filtration on silica gel they were obtained spectroscopically pure in a yield of 60% and with a *E/Z* ratio of about 1:1. If necessary both isomers could be separated by MPLC on silica gel. The *E* and *Z* configurations could be assigned by the chemical shift of the vinyl protons according to increment calculations done for olefinic compounds.[11] An X-ray analysis we recently obtained from a similar compound gave a further proof for the correct structure assignment.[12] From our experience with similar olefinated glycosides we learned that *E*-isomers usually show higher $R_f$-values as the corresponding *Z*-isomers.




Scheme 1

Reagents and conditions: *i*) $PPh_3HBF_4$, $CH_3CN$, reflux, 1 h, quant.; *ii*) BuLi, THF, -90 °C, Garner aldehyde, -90 °C to r.t., 60 %; *iii*) $H_2$ (1 bar), Pd/C 5 %, $CH_3OH$, 2 h, quant.; *iv*) HOAc 70 %, 40 °C, 1 h, 95 %; *v*) $CrO_3$, acetone/3.5 M $H_2SO_4$, 0 °C 0.5h, r.t. 3 h, 86%; *vi* $CH_2N_2$, $CH_3OH$, r.t., quant.

After hydrogenation of unseparated **3a,b** in the presence of palladium on charcoal the β-C compound **4** was obtained as the only isomer in a total yield of 60% starting from phosphonium salt **2a,b**. Because the NMR spectra of **4** showed rotamers the β-configuration was confirmed from $^1H$ NMR spectra of **5**, where 2-Ha shows a quartet at 1.9 - 1.95 ppm with three large coupling constants for $J_{1a,2a}$, $J_{2a,3a}$, $J_{2a,2e}$ in the range of (10-12) Hz.

It is known from literature that similar *N*-Boc acetals can be directly oxidized to *N*-Boc amino acids.[5q] We did not workout the direct oxidation in detail because we were interested in the preparation of the valuable ala-

ninol **5**. The latter in e.g. could be used for the synthesis of a new spiroketal. Further investigations in this area are in progress and will be published in due. In order to obtain amino acid **6** the acetal protective group of *N*-Boc-acetal **4** was splitted off by treatment with acetic acid to give alaninol **5** in nearly quantitative yield. Jones oxidation[13] to amino acid **6** could be performed in a yield of 85%. For further characterization amino acid **6** was transformed quantitatively by treatment with diazomethane into methyl ester **7**.

In conclusion, starting from methyl 3,4,6-tri-*O*-benzyl-2-deoxy-galactopyranoside **1** we obtained glycosyl-amino acid **6** in an overall yield of 46%. The synthesis also can be done without difficulties in g-scale. All products are valuable for further synthetic transformations which are meanwhile in progress.

## Experimental

*General*

The $^{1}H$ and the $^{13}C$ NMR spectra were taken with a Bruker AC 500 spectrometer. The mass spectra including high resolution mass spectra were taken with a Finnigan Model MAT 95 mass spectrometer. IR spectra were recorded with a Bruker IFS 28 spectrometer and $[\alpha]_D$ values were measured with a Perkin-Elmer polarimeter 241 MC. HPLC was done on a LiChrosorb Si 60-column (4x250 mm, 7 µ, Merck) MPLC was performed using silica gel Latek 60 (20µ), a Latek pump system (P-402, 10 bar) and a Latek variable UV detector VISI 6PRAP. Silica gel 60 (70-230 mesh, Merck) was used for column chromatography and silica gel $F_{254}$ plates (Merck) were used for TLC.

**(3,4,6-Tri-*O*-benzyl-2-deoxy-α/β-D-galactopyranosyl)-triphenylphosphonium tetrafluoroborate (2a,b).** A solution of 3,4,6-tri-*O*-benzyl-2-deoxy-methyl-D-galactopyranoside (**1**) (4.50 g, 10 mmol) in absol. acetonitrile (5 mL) was heated with hydrogen triphenylphosphonium tetrafluorborate[8] (3.50 g, 10 mmol) at reflux. After 1 h, the mixture was concentrated in vacuo. The residue was treated with diethyl ether (10 mL) until the remaining oil crystallized. The solid was dried in vacuo (7.60 g, quant.). Crystallization from dichloromethane/toluene gave the pure β-isomer **2b** (3.60 g, 47 %). Further recrystallization from the same solvents afforded satisfactory crystals for an X-ray analysis.[9] The combined filtrates were concentrated in vacuo. The remaining solid was crystallized from dichloromethane/diethyl ether to afford the pure α-isomer **2a** (3.50 g, 46 %). Further recrystallization from the same solvents gave satisfactory crystals for an X-ray analysis.[9]

**2a** α-isomer: mp 163-164 °C; $[\alpha]_D^{20} = -3.9$ ($c$ = 1.04, $CHCl_3$); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ 2.14 (brd, 1H, J = 12.8, 2-Ha), 2.24 (ddd, 1H, J = 2.4, J = 10.1, J = 12.8, 2-Hb), 3.85 (dd, 1H, J = 3.6, J = 6.8, 6-Ha), 3.87 (brs, 1H, 4-H), 4.27 (br, 1H, 3-H), 4.49 (dd, 1H, J = 4.6, J = 6.8, 6-Hb), 4.52 (m, 3H, 5-H, C$\underline{H}_2$Ph), 4.54 (d, 1H, J = 11.6, C$\underline{H}_2$Ph), 4.59 (d, 1H, J = 11.6, C$\underline{H}_2$Ph), 4.62 (d, 1H, J = 12.1, C$\underline{H}_2$Ph), 4.65 (d, 1H, J = 12.1, C$\underline{H}_2$Ph), 5.50 (dt, 1H, J = 2.6, 12.8, 1-H), 7.23-7.40 (m, 15 H, 3 Ph), 7.46-7.65 (m, 6H, Ph), 7.68-7.85 (m, 9H, Ph). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 26.4 (C-2), 63.9 (d, $J_{C\text{-}P}$ = 75.5, C-1), 65.5 (C-6), 71.2 (d, $J_{C\text{-}P}$ = 12.2, C-3), 71.4 (C$\underline{H}_2$Ph), 72.9 (C$\underline{H}_2$Ph), 73.1 (C$\underline{H}_2$Ph), 75.0 $J_{C\text{-}P}$ = 1.4, (C-4) 77.1 (d, $J_{C\text{-}P}$ = 10.9, C-5), 115.5, 116.2, 127.6-

128.9, 130.5, 130.6, 134.2, 134.3, 135.5, 137.9, 138.1 and 138.2 (Ph). IR: ($\nu_{max}$) 1454.4, 1482.0, 1496.8, 2894.6, 3057.2. Anal. Calcd. for $C_{45}H_{44}O_4PBF_4$: C, 70.50; H, 5.79; P, 4.04 Found: C, 70.54; H, 5.80; P, 4.11.

**2b** β-isomer: mp 144-146 °C; $[\alpha]_D^{20}$ = +30.3 (*c* = 1.03, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.03 (dt, 1H, J = 3.3, J = 11.6, 2-Ha), 2.38 (quint, 1H, J = 11.8, 2-Hb), 3.62 (dd, 1 H, J = 8.8, J = 15.8, 6-Ha), 3.64 (dd, 1H, J = 9.5, J = 15.8, 6-Hb), 4.01 (brs, 1H, 4-H), 4.20 (brdd, 1H, J = 3.3, J = 11.0 3-H), 4.24 (t, 1H, J = 6.3, 5-H), 4.46 (s, 2H, C$\underline{H}_2$Ph), 4.52 (d, 1H, J = 10.7, C$\underline{H}_2$Ph), 4.59 (d, 1H, J = 11.5, C$\underline{H}_2$Ph), 4.67 (d, 1H, J = 11.5, C$\underline{H}_2$Ph), 4.95 (d, 1H, J = 10.7, C$\underline{H}_2$Ph), 5.83 (dt, 1H, J = 3.3, 13.0, 1-H), 7,20-7,35 (m, 15 H, 3 Ph), 7.47 (m, 6H, Ph), 7.68-7.85 (m, 9H, Ph). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 27.0 (C-2), 69.3 (C-6), 71.3 (d, $J_{C\text{-}P}$ = 2.9, C-1), 71.6 ($\underline{C}H_2$Ph), 73.3 ($\underline{C}H_2$Ph), 73.5 (C-4), 74.9 ($\underline{C}H_2$Ph), 77.8 (d, $J_{C\text{-}P}$ = 15.9, C-3), 79.6 (d, $J_{C\text{-}P}$ = 12.8, C-5), 116.4, 117.1, 128.0-128.8, 130.6, 130.7, 134.7, 134.8, 135.5, 138.4, 138.6 and 139.3 (Ph). IR: ($\nu_{max}$) 1453.5, 1485.0, 1496.4, 2857.7, 2876.9, 2912.5, 3062.1. Anal. Calcd. for $C_{45}H_{44}O_4PBF_4$: C, 70.50; H, 5.79; P, 4.04 Found: C, 70.52; H, 5.83; P, 3.81.

**(*E/Z*)-4,8-Anhydro-6,7,9-tri-*O*-benzyl-2,3,5-trideoxy-1,2-*N,O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-L-*glycero*-D-*lyxo*-non-3-enitol (3a,b).** To a suspension of α,β-phosphonium salt **2a,b** (770 mg, 1 mmol) in absol. THF (5 mL) at –90 °C n-BuLi (625 μL, 1.6 M in hexane, 1 mmol) was added over a period of 5 min. The Garner aldehyde[10] (230 mg, 1 mmol) in absol. THF (2 mL) was added over a period of 10 min, and the reaction was kept for 1 h at –90 °C and then allowed to come to room temperature overnight. After evaporation in vacuo the solution of the residue in ethyl acetate was washed with water, dried ($MgSO_4$) and concentrated in vacuo. To separate off triphenylphosphine oxide the oily residue was treated with ethyl acetate/diethyl ether filtrated and chromatographed on silica gel (eluent: hexane/ethyl acetate 8:2, containing 0.1 % triethylamine). After evaporation of the solvent in vacuo, **3a,b** was obtained as spectroscopically pure oil (380 mg, 60 %, mixture *E/Z* = 1:1). Separation and purification of the *E/Z* isomers could be afforded by MPLC on silica gel (eluent: hexane/ethyl acetate 8:2, containing 0.1 % triethylamine).

**3a** (*E*)-isomer (spot 1) $[\alpha]_D^{20}$ = +65.6 (*c* = 1.0, $CH_2Cl_2$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 1.30-1.65 (m, 15H, (C(C$\underline{H}_3$)$_2$, C(C$\underline{H}_3$)$_3$), 2.55 (br, 1H, 5-Ha), 2.28 and 3.27 (br, 1H, 5-Hb), 3.55-3.80 (m, 5H, 1-Ha, 6-Ha, 6-Hb, 8-H, 9-H), 3.88 (brs, 1H, 7-H), 3.98 (dd, 1H, J = 6.1, J = 8.4, 1-Hb), 4.42 (brd, 1H, J = 11.8, C$\underline{H}_2$Ph), 4.49 (d, 1H, J = 11.8, C$\underline{H}_2$Ph), 4.55 (m, 1H, 2-H), 4.63 (d, 2H, J = 11.8, C$\underline{H}_2$Ph), 4.75 (brd, 1H, J = 11.8, C$\underline{H}_2$Ph), 4.96 (brd, 1H, J = 11.8, C$\underline{H}_2$Ph), 5.09 (dd, 1H, J = 1.6, J = 10.1, 3-H), 7,20-7,45 (m, 15H, Ph); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 26.2 (C-5), 28.4 and 28.5 (C($\underline{C}H_3$)$_2$, C($\underline{C}H_3$)$_3$), 53.4 (C-1), 54.3 (C-2), 69.5 (C-9), 70.3 ($\underline{C}H_2$Ph), 72.6 (C-7), 73.5 ($\underline{C}H_2$Ph), 74.0 ($\underline{C}H_2$Ph), 77.8 ($\underline{C}$(CH$_3$)$_3$), 78.4, 79.7 (C-6, C-8), 93.0 ($\underline{C}$(CH$_3$)$_2$, 109.5 (C-3), 127.3-128.8, 137.9 and 138.8, (Ph), 149.7, 151.7 (C-4, N$\underline{C}$O); IR: ($\nu_{max}$) 1454.1, 1496.5, 1692.2, 2870.4, 2929.3, 2978.4, 3029.9, 3062.9, 3087.7; MS (FAB, NBA, NaI) m/z (rel. int.): 652.2 ($(M+Na)^+$, 60), 630.2, 628.2, 528.2, 91 (100); HRMS found 652.3256 (M+Na); calc. for $C_{38}H_{47}NO_7Na$ 652.3250.

**3b** (*Z*)-isomer (spot 2) $[\alpha]_D^{20}$ = +47.5 (*c* = 0.73, $CH_2Cl_2$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 1.30-1.65 (m, 15H,

($C(C\underline{H}_3)_2$, $C(C\underline{H}_3)_3$), 2.38 (dd, 1H, J = 4.2, J = 13.2, 5-Ha), 2.77 (dd, 1H, J = 11.8, J = 13.2, 5-Hb), 3.60-3.70 (m, 5H, 1-Ha, 6-Ha, 6-Hb, 8-H, 9-H), 3.95 (brs, 1H, 7-H), 3.99 (dd, 1H, J = 6.5, J = 7.8, 2-H), 4.47 (d, 1H, J = 11.8, $C\underline{H}_2Ph$), ), 4.50 (d, 1H, J = 11.8, $C\underline{H}_2Ph$), 4.55 (m, 3H, 1-Hb, $C\underline{H}_2Ph$), 4.63 (d, 1H, J = 11.8, $C\underline{H}_2Ph$), 4.70 (br, 1H, 3-H), 4.95 (d, 1H, J = 11.8, $C\underline{H}_2Ph$), 7,20-7,45 (m, 15H, Ph); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 28.5 ($C(\underline{C}H_3)_2$, $C(\underline{C}H_3)_3$), 31.0 (C-5), 69.2 (C-9), 69.4 (C-1), 70.3 ($\underline{C}H_2Ph$), 72.6 (C-2, C-7), 73.5 ($\underline{C}H_2Ph$), 74.0 ($\underline{C}H_2Ph$), 78.2, 79.5 (C-6, C-8, $\underline{C}(CH_3)_3$), 93.5 ($\underline{C}(CH_3)_2$, 111.3 (C-3), 127.3-128.8, 134.4, 137.9, 138.2 and 138.8, (Ph), 149.7, 152.0 (C-4, $N\underline{C}O$); IR: ($\nu_{max}$) 1454.1, 1496.5, 1693.9, 2870.6, 2932.1, 2979.2, 3030.6, 3063.6, 3088.2; MS (FAB, NBA + NaI) m/z (rel. int.): 652.2 ($(M+Na)^+$, 100), 630.2, 628.2, 528.2, 91.0 (40); HRMS found 652.3255 (M+Na); calc. for $C_{38}H_{47}NO_7Na$ 652.3250.

**β-(3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-*N,O*-isopropylidene-D-alaninol (4).** To a solution of **3a,b** (631 mg, 1 mmol) in methanol containing 0.1 % triethylamine was added Pd/C 5 % (100 mg). The mixture was hydrogenated for 2 h at 1 bar. After filtration and evaporation in vacuo. the residue was filtrated on silica gel (hexane/ethyl acetate 8:2) to afford compound **4** as a pure oil, yield 630 mg (quant.). HPLC (hexane/ethyl acetate 8:2) $t_R$ = 4.8 min (>98 %); $[\alpha]_D^{21}$ = -5.2 (*c* = 0.95, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, 330 K) δ 1.44 and 1.52 (2s, 15H, $C(C\underline{H}_3)_2$, $(C(C\underline{H}_3)_3)$, 1.52-1.94 (m, 4H, β-$C\underline{H}_2$, 2-$C\underline{H}_2$), 3.30-3.61 (m, 5H, 1-H, 3-H, 5-H, 6-$C\underline{H}_2$), 3.83 (m, 3H, 4-H, $C\underline{H}_2O$), 4.07 (br, 1H, α-$C\underline{H}N$), 4.42 (d, 1H, J = 11.9, $C\underline{H}_2Ph$), 4.48 (d, 1H, J = 11.9, $C\underline{H}_2Ph$), 4.53 (d, 1H, J = 11.6, $C\underline{H}_2Ph$), 4.59 (s, 2H, $C\underline{H}_2Ph$), 4.85 (d, 1H, J = 11.6, $C\underline{H}_2Ph$), 7,20-7,35 (m, 15H, Ph); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 28.4 ($C(\underline{C}H_3)_2$, $C(\underline{C}H_3)_3$), 32.8 (C-6), 39.1 (C-β), 54.3 (C-α), 68.2 ($\underline{C}H_2OH$), 71.1 (C-6), 71.4 ($\underline{C}H_2Ph$), 74.7 (C-4, C-1), 74.5 ($\underline{C}H_2Ph$), 75.5 ($\underline{C}H_2Ph$), 78.8, 79.9 (C-3, C-5), 80.3 ($\underline{C}(CH_3)_3$), 93.5 ($\underline{C}(CH_3)_2$), 128.4-129.4, 138.1, 138.5, and139.4, (Ph), 151.8 ($N\underline{C}O$); IR: ($\nu_{max}$) 1454.1, 1496.5, 1694.1, 2866.8, 2927.8, 2976.6, 3029.6, 3063.0, 3087.8; MS (FAB) m/z (rel. int.): 632.4 ($MH^+$, 20), 532.3 (50), 91.0 (100); Anal. Calcd. for $C_{38}H_{49}NO_7$: C, 72.24; H, 7.82; N, 2.22. Found: C, 72.26; H, 7.86; N, 2.22.

**β-(3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-*galacto*pyranosyl)-*N*-*tert*-butoxycarbonyl-D-alaninol (5).** Compound **4** (635 mg, 1 mmol) was treated with 70 % aq. acetic acid (20 mL) at 40 °C for about 2 h until the reaction was complete (monitored by TLC, hexane/ethyl acetate 7:3). The solution was concentrated in vacuo and the remaining oil was dissolved in dichloromethane (20 mL) and washed successively with saturated $NaHCO_3$ and water. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by MPLC (eluent: hexane/ethyl acetate 1:1) to afford *N*-BOC amino alcohol **5** as a analytically pure oil (565 mg, 95%). HPLC (hexane/ ethyl acetate 1:1) $t_R$ = 7.0 min (>98%); $[\alpha]_D^{20}$ = -24.0 (*c* = 1.0, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H, $(C(C\underline{H}_3)_3)$, 1.78 (ddd, 1H, J = 5.2, J = 8.9, J = 14.8, β-$C\underline{H}$a), 1.83, (brd, 1H, J = 12.0, 2-He), 1.87 (ddd, 1H, J = 2.0, J = 5.8, J = 14.8, β-$C\underline{H}$b), 1.95 (q, 1H, J = 12.0, 2-Ha), 2.16 (s, 1H, OH); 3.33 (dd, 1H, J = 5.0, J = 8.8, 6-Ha), 3.45 (dd, 1H, J = 2.0, J = 10.2, 3-H), 3.48-3.57 (m, 3H, 1-H, 5-H, 6-Hb),

3.58 (dd, 1H, J = 4.2, J = 11.5, CHaOH), 3.68 (dd, 1H, J = 3.00, J = 11.5, CHbOH), 3.76 (br, 2H, 4-H, α-CHN), 4.39 (d, 1H, J = 11.9, $CH_2Ph$), 4.48 (d, 1H, J = 11.9, $CH_2Ph$), 4.59 (d, 1H, J = 12.2, $CH_2Ph$), 4.61 (d, 1H, J = 12.2, $CH_2Ph$), 4.62 (d, 1H, J = 11.9, $CH_2Ph$), 4.90 (d, 1H, J = 11.9, $CH_2Ph$), 5.33 (brd, 1H, J = 5.0, NH), 7,20-7,40 (m, 15H, Ph); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 28.4 ($C(CH_3)_3$), 32.8 (C-6), 38.0 (C-β), 50.2 (C-α), 65.2 ($CH_2OH$), 69.9 (C-6), 70.2 ($CH_2Ph$), 72.0 (C-4), 73.0 (C-1), 73.6 ($CH_2Ph$), 74.1 ($CH_2Ph$), 77.7, 78.4 (C-3, C-5), 79.3 ($C(CH_3)_3$), 127.3-128.5, 137.7, 138.3, and138.6, (Ph), 156.1 (NCO); IR: ($\nu_{max}$) 1454.1, 1496.5, 1695.8, 2341.0, 2360.3, 2866.5, 2926.0, 2974.0, 3030.0, 3063.0, 3087.8; MS (FAB) m/z (rel. int.): 592.3 ($MH^+$, 20), 492.2 (50), 91.0 (100); Anal. Calcd. for $C_{35}H_{45}NO_7$: C, 71.04; H, 7.66; N, 2.37. Found: C, 70.68; H, 7.65; N, 2.36.

**β-(3,4,6-Tri-*O*-benzyl-2-deoxy-ß-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine (6).** At 0 °C a solution of $CrO_3$ (76 mg, 0.76 mmol) in $H_2SO_4$ (3 mL, 3.5 M) was added to amino alcohol **5** (96 mg, 0.162 mmol) dissolved in acetone (3 mL). Stirring was continued at 0 °C for 0.5 h then at room temperature for 3 h. After addition of $NaHCO_3$ to pH 6 the reaction mixture was extracted with ethyl acetate. The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo to give amino acid **6** as spectroscopically pure oil, yield 84.5 mg (86 %). $[\alpha]_D^{20}$ = -24.5 (*c* = 1.45, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H, ($C(CH_3)_3$), 1.82, (br, 1H, 2-He), 1.90 (q, 1H, J = 11.8, 2-Ha), 2.00-2.06 (m, 2H, β-$CH_2$), 3.47-3.56 (m, 5H, 1-H, 3-H, 5-H, 6-Ha 6-Hb), 3.83 (s, 1H, 4-H), 4.31 (m, 1H, α-CHN), 4.37 (d, 1H, J = 11.8, $CH_2Ph$), 4.45 (d, 1H, J = 11.8, $CH_2Ph$), 4.55 (d, 1H, J = 12.1, $CH_2Ph$), 4.58 (d, 1H, J = 12.1, $CH_2Ph$), 4.61 (d, 1H, J = 11.7, $CH_2Ph$), 4.90 (d, 1H, J = 11.7, $CH_2Ph$), 5.46 (brd, 1H, J = 4.7, NH), 7,20-7,35 (m, 15H, Ph), 9.1 (br, 1H, COOH); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 28.3 ($C(CH_3)_3$), 32.3 (C-6), 37.1 (C-β), 51.7 (C-α), 69.2 (C-6), 70.1 ($CH_2Ph$), 72.2 (C-4), 73.4 ($CH_2Ph$), 73.6 (C-1), 74.2 ($CH_2Ph$), 77.4, 78.2 (C-3, C-5), 80.1 ($C(CH_3)_3$), 127.3-128.7, 137.9, 138.3, and 138.6, (Ph), 155.9 (NCO), 175.4 (COOH); IR: ($\nu_{max}$) 1453.1, 1497.5, 1701.1, 2925.2, 3406.1 ($H_2O$); MS (FAB) m/z (rel. int.): 604.3 ($(M-H)^+$, 100), 530.1 (100); HRMS found 604.2943 (M-H); calc. for $C_{35}H_{42}NO_8$ 604.2910.

**Methyl β-(3,4,6-tri-*O*-benzyl-2-deoxy-ß-D-galactopyranosyl)-*N*-*tert*-butoxycarbonyl-D-alanine (7).** Amino acid **6** (50 mg, 0.082 mmol) dissolved in methanol was treated with diazomethane until esterification was complete (monitored by TLC). Evaporation in vacuo and filtration on silica gel (eluent: hexane/ethyl acetate 6:3) afforded analytically pure amino acid ester **7** (51 mg, quant.). HPLC (hexane/ethyl acetate 8:2) $t_R$ = 7.4 min (>98 %); $[\alpha]_D^{20}$ = -21.4 (*c* = 0.94, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H, ($C(CH_3)_3$), 1.82, (brd, 1H, J = 11.5, 2-He), 1.90 (q, 1H, J = 11.7, 2-Ha), 1.95-2.08 (m, 2H, β-$CH_2$), 3.40-3.57 (m, 5H, 1-H, 3-H, 5-H, 6-Ha 6-Hb), 3.66 (s, 3H, $OCH_3$), 3.86 (s, 1H, 4-H), 4.32 (q, 1H, J = 6.1, α-CHN), 4.39 (d, 1H, J = 11.7, $CH_2Ph$), 4.46 (d, 1H, J = 11.7, $CH_2Ph$), 4.57 (s, 2H, $CH_2Ph$), 4.61 (d, 1H, J = 11.7, $CH_2Ph$), 4.90 (d, 1H, J = 11.7, $CH_2Ph$), 5.36 (brd, 1H, J = 6.7, NH), 7,20-7,40 (m, 15H, Ph); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 28.3

($C(\underline{C}H_3)_3$), 32.5 (C-6), 37.7 (C-β), 51.4 (C-α), 52.2 ($\underline{C}H_3OOC$), 69.1 (C-6), 70.1 ($\underline{C}H_2Ph$), 72.3 (C-4), 73.0 (C-1), 73.5 ($\underline{C}H_2Ph$), 74.3 ($\underline{C}H_2Ph$), 77.2, 78.3 (C-3, C-5, $\underline{C}(CH_3)_3$), 127.3-128.4, 138.0, 138.4, and 139.0, (Ph), 155.4 (N$\underline{C}$O), 172.9 ($\underline{C}$OOMe); IR: ($\nu_{max}$) 1453.9, 1496.8, 1713.9, 1743.5, 2864.8, 2927.0, 2975.3, 3029.6, 3062.4, 3087.5; MS (FAB) m/z (rel. int.): 592.3 ($MH^+$ , 20), 492.2 (50), 91.0 (100); Anal. Calcd. for $C_{36}H_{45}NO_8$: C, 69.77; H, 7.32; N, 2.26. Found: C, 69.77; H, 7.38; N, 2.14.

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