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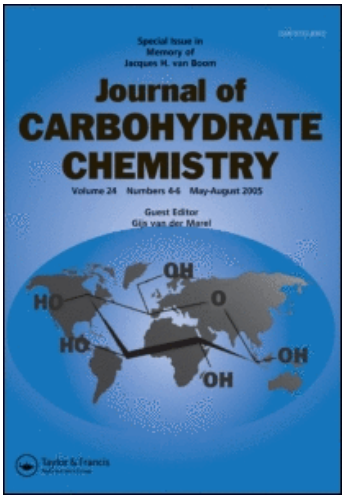

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SYNTHESIS OF AMINOACYL SUGAR DERIVATIVES AND THEIR TASTE CHARACTERISTICS. I. 2,3-DI-*O*-AMINOACYL DERIVATIVES OF ALKYL D-GLUCOPYRANOSIDES

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ABSTRACT

Aminoacyl derivatives of methyl α- and β-D-glucopyranosides have been synthesized in order to ascertain the structural features required for the perception of a sweet taste. 2,3-Di-*O*-(L-aminoacyl) derivatives of methyl α-D-glucopyranoside showed a strong sweet taste (16–35× sucrose), which decreased or disappeared when either one of the two L-aminoacyl groups was absent or substituted by a D-aminoacyl group. In the case of 2,3-di-*O*-(L-alanyl) derivatives of methyl D-glucopyranoside, the α-anomer was very sweet (16–25× suc.) whereas the β-anomer was not sweet. The structural prerequisite for sweetness in this group of compounds proved to be the presence of L-aminoacyl groups at C-2 and C-3, and the α-configuration at C-1. Its α-isopropyl anomer showed the highest sweetness (64× suc.), hence the increased lipophilicity is also an important criterion.

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INTRODUCTION

Sweet tasting organic compounds, most of them discovered by serendipity, all have an essential molecular feature with a bifunctional entity of AH_s and B_s units, where the AH_s is a proton donating group, closely positioned (2.5–4.0 Å) to the B_s, a proton accepting group.[1] This unit binds to the receptor in conjunction with a hydrophobic site (X_s) which plays a role of intensifying the sweet sensation.[2] A clockwise arrangement of this $AH_s/B_s/X_s$ triad is required to allow completion of three-point coupling with a reciprocal $AH_r/B_r/X_r$ function by stereospecific interaction with the receptor.[3] Molecular modeling of interactions between various sweet compounds and an α-helical proteinaceous receptor model have been studied, and accounts for the tastant-receptor mechanism for sweet taste perception and intensity in amino acids,[4] sugars,[5] aspartame,[6] sucronic acid,[7] sucralose and related compounds.[8]

As an extension of the helical receptor theory in the design of new sweeteners, we have investigated the methyl 2,3-di-*O*-(L-aminoacyl)-α-D-glucopyranosides reported by Okai et al.[9] In this series of papers, several methyl α-D-glucopyranosides having the same L-aminoacyl group at both of C-2 and C-3 positions were sweet, whilst, on the other hand, D-aminoacyl derivatives, such as the 2,3-di-*O*-(D-alanyl) derivative, were bitter without a sweet taste. Hence the structural feature present in such compounds for the initiation of sweet taste appears to be a combination of AH_s/B_s units in the L-amino acid residues for hydrogen bonding, whilst utilizing the pyranoside skeleton for a favorable stereochemical interaction with the receptor.

In this article, we describe the syntheses of mono- and di-*O*-(aminoacyl) derivatives of α- and β-D-glucopyranosides, their structure-taste characteristic relationships and the structural requirements for the perception of sweet taste in these compounds.

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RESULTS AND DISCUSSION

Synthesis of Aminoacyl Sugar Derivatives

The readily available methyl 4,6-*O*-benzylidene-α-D-glucopyranoside[10] was used as the starting material for the preparation of various methyl *O*-(aminoacyl)-α-D-glucopyranosides. Regioselective acylation[11] of the starting material with 1-(*N*-Boc-aminoacyl)-1*H*-benzotriazole, generated in situ, afforded the 2-*O*-(*N*-Boc-L-aminoacyl) derivatives **1** and **13** as the major products respectively. However, under conventional carbodiimide mediated condensation, the 3-*O*-(*N*-Boc-L-aminoacyl) derivative **4** was obtained predominantly (over 50% yield) along with the 2,3-di-*O*-(aminoacyl) derivative (∼12%). The mixed 2,3-di-*O*-(aminoacyl) derivatives **7**, **10** and **14** were prepared from the 2-*O*-aminoacyl derivatives **1** and **13** by further condensations with different N-protected amino acids. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(*N*-Boc-L-alanyl)-β-D-glucopyranoside (**17**) was derived analogously. ^{1}H NMR spectra of the aminoacylated sugars clearly revealed the positions of acylation by characteristic down field shifts of the corresponding ring protons, at C-2 and C-3. Isopropyl 2,3-di-*O*-(*N*-Boc-L-alanyl)-α-D-glucopyranoside (**20**) was prepared starting from isopropyl α-D-glucopyranoside[12] through 4,6-*O*-benzylidenation and conventional 2,3-di-*O*-acylation. Each of the *O*-aminoacyl derivatives of methyl α- and β-D-glucopyranosides was examined for its taste as the hydrochlorides (**2**, **5**, **8**, **11**, **15**, **18**, **21**); they were

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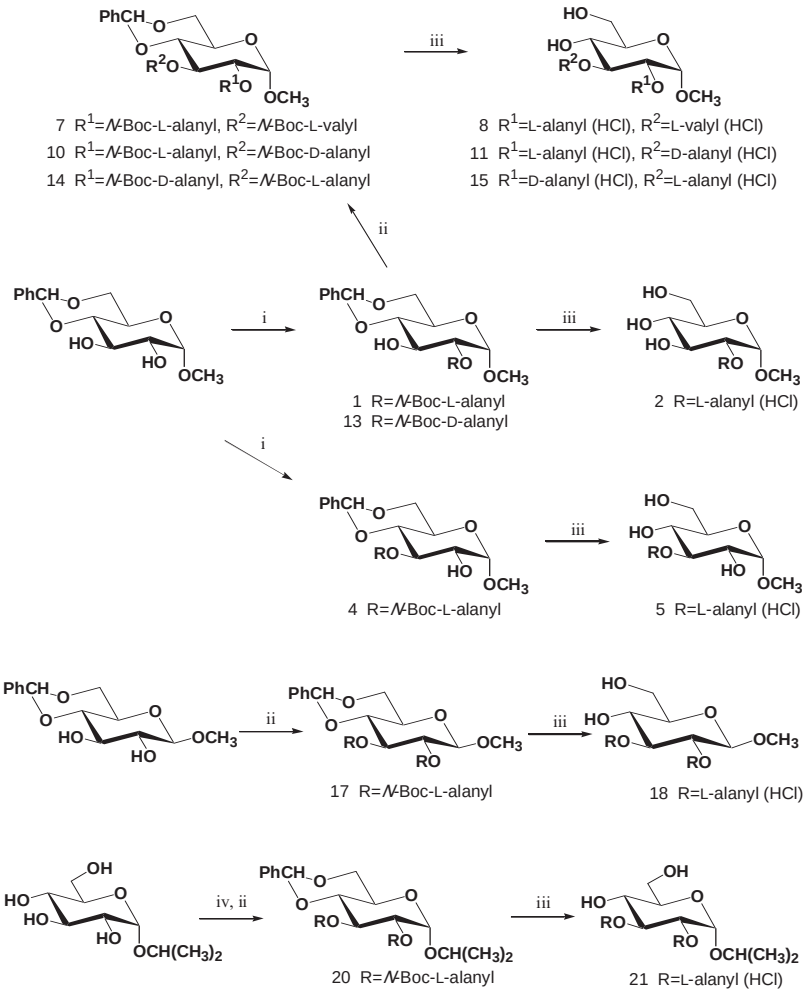

i) *N*-Boc-amino acid/EDCI/HOBt/base, ii) *N*-Boc-amino acid/EDCI/base,
iii) HCl/dioxane, iv) $PhCH(OCH_3)_2$/*p*-TsOH/DMF.

Scheme 1.

prepared by treatment of their protected derivatives, **1**, **4**, **7**, **10**, **14**, **17**, **20** with HCl in dioxane, and purified by passage through highly porous resin, and then lyophilized (Scheme 1). All of the aminoacylated hydrochlorides examined tastes were converted into their crystalline peracyl derivatives (**3**, **6**, **9**, **12**, **16**, **19**, **22**) for further confirmation of their structures.

Structure–Taste Characteristics Relationship

Table 1 gives taste characteristics of the various aminoacyl derivatives of D-glucopyranoside that have been synthesized. Amongst the L-alanyl derivatives, only the

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Table 1. Taste Characteristics of *O*-aminoacyl-D-glucopyranoside Hydrochlorides

Compounds	Taste Characteristics[a]
Methyl 2,3-di-*O*-(L-alanyl)-α-D-glucopyranoside	sweet (16–25 × sucrose)
Methyl 2-*O*-(L-alanyl)-α-D-glucopyranoside (**2**)	not sweet
Methyl 3-*O*-(L-alanyl)-α-D-glucopyranoside (**5**)	not sweet
Methyl 2-*O*-(L-alanyl)-3-*O*-(L-valyl)-α-D-glucopyranoside (**8**)	sweet (35 × sucrose)
Methyl 2,3di-***O***-(D-alanyl)-α-D-glucopyranoside	bitter
Methyl 3-*O*-(D-alanyl)-2-*O*-(L-alanyl)-α-D-glucopyranoside (**11**)	slightly sweet (8 × sucrose) with bitter
Methyl 2-*O*-(D-alanyl)-3-*O*-(L-alanyl)-α-D-glucopyranoside (**15**)	not sweet and weakly bitter
Methyl 2,3-di-*O*-(L-alanyl)-β-D-glucopyranoside (**18**)	not sweet
Methyl 2,3-di-*O*-(L-alanyl)-α-D-glucopyranoside (**21**)	sweet (64–85 × sucrose)

[a] Tastes were examined by a panel of five people. The sweet taste potencies were determined by ratios of threshold values of compounds in aqueous solutions compared to the value of sucrose (4% w/v).

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2,3-di-*O*-(L-alanyl) derivative of the α-anomer showed significant sweetness (16–25× sucrose).[13] An increase in sweetness intensity was observed in mixed di-*O*-(L-aminoacyl) derivatives when a slightly more hydrophobic amino acid residue was introduced at C-3, such as the 2-*O*-(L-alanyl)-3-*O*-(L-valyl) derivative **8** (35× sucrose). Reduced sweet taste potency was shown in mono-*O*-(L-alanyl) derivatives, **2** and **5**, which lacked one of the two L-alanyl groups. The importance of amino acid chirality was illustrated by the mixed D- and L-alanyl derivatives **11** (sweet, 8× sucrose.) and **15** (bitter with non-sweet taste). These results suggested that the principal structural prerequisite for significant sweetness was the presence of two vicinal L-aminoacyl groups attached to the pyranoside ring at C-2 and C-3. The chirality of the amino acid residue at C-2 was especially critical, the L-configuration giving rise to a sweet taste and the D-configuration a bitter taste. In molecular recognition by the sweet taste receptor, D-amino acids are usually sweet and L-amino acids are not sweet or less sweet, but the reverse stereospecificity has now been observed for the amino acid residues present in the above aminoacyl derivatives of α-D-glucopyranoside. Comparison of the α- and β-anomers of methyl 2,3-di-*O*-(L-alanyl)-D-glucopyranoside revealed that only the α-anomer was sweet, an additional prerequisite for sweetness at the hydrophobic sites. Furthermore, increased

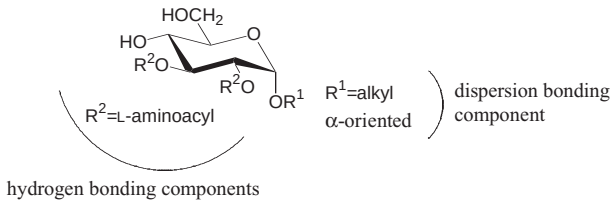

Figure 1. Structural features for sweet tasting aminoacyl sugar derivatives.

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lipophilicity of the favorable α-anomeric centre increased the sweetness intensity as shown by the α-isopropyl derivative (**21**).

CONCLUSIONS

The essential molecular requirements for sweet taste perception in aminoacylated glucopyranosides are shown to be two vicinal L-aminoacyl groups at C-2 and C-3, as originally described by Okai et al.[9] with the additional requirement of an α-oriented 1-*O*-alkyl group attached to the pyranoside ring. Thus the molecular recognition mechanism of these sweet tasting aminoacyl glucopyranosides by the glycophoric receptor is highly stereospecific with two vicinal L-aminoacyl groups serving as hydrogen bonding components (AH_s and B_s) and an α-alkoxy group acting as the dispersion bonding component, X_s (Figure 1). Increased hydrophobicity of X_s provides a more stable dispersive interaction with the receptor for enhanced sweetness potency, as observed for isopropyl 2,3-di-*O*-(L-alanyl)-α-D-glucopyranoside (**21**).

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EXPERIMENTAL

General Procedures. Melting points were determined in capillary tubes using a Yazawa apparatus and are uncorrected. Optical rotations were measured using the JASCO Digital Polarimeter (DIP 1000, path length 10 cm). Mass spectra were measured by Hitachi M-180 (70 eV). ^{1}H NMR spectra were recorded on a JEOL JNM-A500 spectrometer and assignments were facilitated by decoupling methods. Elemental analyses were performed on a Perkin–Elmer 2400 II elemental analyzer. Preparative column chromatography was carried out on silica gel (Wako, 200 mesh) with the solvent systems specified. Highly porous resin chromatography was performed with Diaion HP-20 resin (Mitsubishi Kasei Co.) using water as the eluent.

Methyl 4,6-*O*-benzylidene-2-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-α-D-glucopyranoside (1). 1-Hydroxybenzotriazole (1.91 g, 14.1 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, 2.71 g, 14.2 mmol) were added to a solution of Boc-L-alanine (2.68 g, 14.2 mmol) in tetrahydrofuran (30 mL), and the mixture was stirred at room temperature for 30 min. A solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (2.0 g, 7.1 mmol) in pyridine (17.5 mL) and tetrahydrofuran (20 mL) was added in one portion, and stirring was continued overnight. After concentration of the reaction mixture, the residue was dissolved in chloroform (200 mL) and washed sequentially with a 4% sodium hydrogen carbonate solution (140 mL×3), water (120 mL), a 5% sodium hydrogen sulfate solution (100 mL×3), and then water (80 mL×3). The organic layer was dried and concentrated, and the residue was crystallized from ethyl acetate to give **1** (2.32 g, 72%): mp 182–184 °C; $[\alpha]_D^{25}$ +66.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.43 (d, 3H, J = 6.8 Hz, alanyl-CH_3), 1.45 (s, 9H, t-butyl), 3.40 (s, 3H, 1-OCH_3), 3.57 (t, 1H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 3.77 (t, 1H, $J_{5,6a} = J_{6a,6b} =$ 10.4 Hz, H-6a), 3.86 (dt, 1H, $J_{5,6b} = 4.9$ Hz, H-5), 4.17 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-3), 4.30 (dd, 1H, H-6b), 4.34 (q, 1H, J = 6.7 Hz, alanyl-CH), 4.87 (dd, 1H, H-2), 4.90 (d, 1H, $J_{1,2} =$ 3.0 Hz, H-1), 5.55 (s, 1H, Ph-CH), 7.35–7.38 and 7.48–7.50 (each m, 3H and 2H, Ph).

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Anal. Calcd for $C_{22}H_{31}NO_9$ (453.48); C, 58.27; H, 6.89; N, 3.09%. Found; C, 58.50; H, 7.05; N, 2.99%.

Methyl 2-*O*-(L-alanyl)-α-D-glucopyranoside hydrochloride (2) and Methyl 3,4,6-tri-*O*-benzoyl-2-*O*-(*N*-benzoyl-L-alanyl)-α-D-glucopyranoside (3). A solution of **1** (1.5 g, 3.3 mmol) in 4M HCl in dioxane (12 mL) was stirred at room temperature for 2 h and diluted with isopropyl ether (60 mL). The precipitate that formed was collected and dissolved in water (12 mL). The aqueous solution was subjected to highly porous resin chromatography and the product was eluated with water. The eluates, which showed a positive ninhydrin test, were collected and lyophilized to afford of **2** (733 mg, 69%) as an amorphous powder: $[\alpha]_D^{20}$ + 127° (*c* 1.0, methanol); ^{1}H NMR (D_2O) δ 1.46 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 3.26 (s, 3H, 1-OCH_3), 3.38 (t, 1H, $J_{3,4} = J_{4,5} = 9.45$ Hz, H-4), 3.54 (ddd, 1H, H-5), 3.63 (dd, 1H, $J_{5,6a} = 5.5$ Hz, $J_{6a,6b} = 12.2$ Hz, H-6a), 3.74 (dd, 1H, $J_{5,6b} = 1.8$ Hz, H-6b), 3.73 (t, 1H, $J_{2,3} = 9.45$ Hz, H-3), 4.11 (q, 1H, J = 7.3 Hz, alanyl-CH), 4.75 (dd, 1H, H-2), 4.86 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1).

Anal. Calcd for $C_{10}H_{20}ClNO_7$ H_2O (319.74); C, 37.56; H, 6.93; N, 4.38%. Found; C, 37.47; H, 7.10; N, 4.08%.

Benzoylation of **2** (400 mg, 1.3 mmol) with benzoyl chloride (0.91 mL) in pyridine (6 mL) gave **3** (580 mg, 65%) as colorless needles: mp 149–151 °C (from EtOAc); $[\alpha]_D^{20}$ + 34.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDC1_3$) δ 1.26 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 3.52 (s, 3H, 1-OCH_3), 4.39 (ddd, 1H, $J_{5,6a} = 5.5$ Hz, $J_{5,6b} = 3.0$ Hz, H-5), 4.47 (dd, 1H, $J_{6a,6b} = 12.2$ Hz, H-6a), 4.59 (dd, 1H, H-6b), 4.82 (q, 1H, J = 7.3 Hz, alanyl-CH), 5.09 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.25 (dd, 1H, $J_{2,3} = 9.7$ Hz, H-2), 5.63 (t, 1H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 6.06 (t, 1H, H-3), 6.09 (broad d, 1H, J = 7.9 Hz, alanyl-NH), 7.30–8.04 (m, 20H, 4×Ph).

Anal. Calcd for $C_{38}H_{35}NO_{11}$ (681.69); C, 66.95; H, 5.18; N, 2.05%. Found; C, 67.03; H, 5.24; N, 2.04%.

Methyl 4,6-*O*-benzylidene-3-*O*-(*N*-t-butoxycarbonyl-L-alanyl)-α-D-glucopyranoside (4). To a stirred mixture of *N*-Boc-L-alanine (2.0 g, 10.6 mmol) and EDCI (2.0 g, 10.6 mmol) in tetrahydrofuran (30 mL) was added a solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (2.0 g, 7.1 mmol) in pyridine (17.5 mL) and tetrahydrofuran (20 mL), and the mixture was stirred at room temperature for 2 days. The reaction mixture was then concentrated in vacuo, the residue was dissolved in ethyl acetate (250 mL), and washed sequentially with a 5% sodium hydrogen sulfate solution (150 mL×3), water (120 mL), a 4% sodium hydrogen carbonate solution (150 mL×3), and then water (100 mL×3). After the organic layer was dried and concentrated, the residue was chromatographed on a silica gel column to give of **4** (1.8 g, 54%) as a syrup: $[\alpha]_D^{25}$ + 68.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.43 (d, 3H, J = 7.4 Hz, alanyl-CH_3), 1.45 (s, 9H, t-butyl), 3.47 (s, 3H, 1-OCH_3), 3.63 (dd, 1H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 3.69 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-2), 3.76 (dd, 1H, $J_{5,6a} = J_{6a,\ 6b} = 10.4$ Hz, H-6a), 3.88 (ddd, 1H, H-5), 4.31 (dd, 1H, H-6b), 4.33 (q, 1H, J = 7.3 Hz, alanyl-CH), 4.82 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.36 (t, 1H, H-3), 5.50 (s, 1H, Ph-CH), 7.3-7.35 (m, 5H, Ph).

Anal. Calcd for $C_{22}H_{31}NO_9$ H_2O (471.50); C, 56.04; H, 7.05; N, 2.97%. Found; C, 56.32; H, 6.91; N, 3.28%.

Methyl 3-*O*-(L-alanyl)-α-D-glucopyranoside hydrochloride (5) and Methyl 2,6-di-*O*-biphenylcarbonyl-3-*O*-(*N*-biphenylcarbonyl-L-alanyl)-α-D-glucopyranoside

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(6). Compound **4** (50 mg, 0.11 mmol) was treated with HCl in dioxane (0.4 mL) and the mixture was concentrated to give of **5** (25 mg, 71%) as a colorless syrup: $[\alpha]_D^{21}$ + 95.2° (*c* 1.0, water); ^{1}H NMR (D_2O) δ 1.42 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 3.29 (s, 3H, 1-OCH_3), 3.50 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 3.59 (ddd, 1H, $J_{5,6a} = 4.9$ Hz, $J_{5,6b} = 1.8$ Hz, H-5), 3.63 (dd, 1H, $J_{6a,6b} = 12.2$Hz, H-6a), 3.72 (dd, 1H, H-6b), 4.12 (q, 1H, J = 7.3 Hz, alanyl-CH), 4.60-4.63 (dd, 1H, H-2), 4.70 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.05 (t, 1H, $J_{2,3} = 9.8$ Hz, H-3).

Anal. Calcd for $C_{10}H_{20}ClNO_7$ H_2O (319.74); C, 37.56; H, 6.93; N, 4.38%. Found; C, 37.91; H, 6.78; N, 4.62%.

The above syrup **5** (156 mg, 0.5 mmol) was treated with biphenylcarbonyl chloride in pyridine to give crystalline **6** (124 mg, 31%): mp 200–203 °C (from EtOAc); $[\alpha]_D^{19}$ + 37.0° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.35 (d, 3H, J = 6.7 Hz, alanyl-CH_3), 3.46 (s, 3H, 1-OCH_3), 3.92 (dd, 1H, $J_{4,5} = 9.8$ Hz, H-4), 4.14 (ddd, 1H, H-5), 4.59 (q, 1H, J = 6.7 Hz, alanyl-CH), 4.71 (dd, 1H, $J_{5,6a} = 2.4$ Hz, $J_{6a,6b} = 12.2$ Hz, H-6a), 4.77 (dd, 1H, $J_{5,6b} = 4.8$ Hz, H-6b), 5.13 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.18 (dd, 1H, $J_{2,3} = 10.4$ Hz, H-2), 5.76 (dd, 1H, $J_{3,4} = 9.1$ Hz, H-3), 6.71 (broad d, 1H, NH), 7.38–8.17 (27H, 3× biphenyl).

Anal. Calcd for $C_{49}H_{43}NO_{10}$ (805.88); C, 72.95; H, 5.47; N, 1.74%. Found; C, 73.03; H, 5.38; N, 1.74%.

Methyl 4,6-*O*-benzylidene-2-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-3-*O*-(*N*-*t*-butoxycarbonyl-L-valyl)-α-D-glucopyranoside (7). To a stirred mixture of *N*-Boc-L-valine (2.15 g, 9.9 mmol) and EDCI (2.84 g, 14.9 mmol) in dichloromethane (22 mL) was added a solution of **1** (1.5 g, 3.3 mmol) and 4-dimethylaminopyridine (DMAP, 200 mg, 1.65 mmol) in dichloromethane (15 mL). The reaction mixture was stirred at room temperature overnight and washed with a 5% sodium hydrogen sulfate solution (22 mL×3), water (22 mL), a 5% sodium hydrogen carbonate solution (22 mL×3), and water (22 mL), then concentrated. The residual syrup was purified by column chromatography and crystallized from ethyl acetate to give of **7** (990 mg, 46%) as colorless needles: mp 140–141 °C; $[\alpha]_D^{25}$ + 17.8° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.81 and 0.90 (2×d, each 3H, J = 6.7 Hz, 2×valyl-CH_3), 1.35 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 1.44 (18H, 2× *t*-butyl), 2.25 (m, 1H, valyl β-CH), 3.43 (s, 3H, 1-OCH_3), 3.70 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 3.78 (t, 1H, H-6a), 3.94 (ddd, 1H, $J_{5,6a} = 10.4$ Hz, $J_{5,6b} = 4.9$ Hz, H-5), 4.21 (dd, $J_{\alpha\text{-CH},\beta\text{-CH}} = 5.5$ Hz, $J_{\alpha\text{-CH,NH}} = 9.1$ Hz, valyl α-CH), 4.33 (dd, 1H, H-6b), 4.37 (q, 1H, J = 7.3 Hz, alanyl-CH), 4.91 (d, 1H, $J_{NH,\alpha\text{-CH}} = 9.1$ Hz, valyl-NH), 4.94 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.01 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-2), 5.12 (d, 1H, alanyl-NH), 5.51 (s, 1H, Ph-CH), 5.64 (t, 1H, H-3), 7.32-7.47 (5H, Ph).

Anal. Calcd for $C_{32}H_{48}N_2O_{12}$ (652.73); C, 58.88; H, 7.41; N, 4.29%. Found; C, 58.86; H, 7.56; N, 4.38%.

Methyl 2-*O*-(L-alanyl)-3-*O*-(L-valyl)-α-D-glucopyranoside dihydrochloride (8). Compound **7** (830 mg, 1.3 mmol) was treated with HCl / dioxane giving **8** (330 mg, 57%) as colorless needles (from EtOH-hexane): mp 195 °C (dec.); $[\alpha]_D^{21}$ + 162° (*c* 1.0, water); ^{1}H NMR (DMSO-d_6) δ 0.96 and 0.97 (2×d, each 3H, J = 7.4 Hz, 2×valyl-CH_3), 1.36 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 2.20 (m, 1H, valyl β-CH), 3.40 (s, 3H, 1-OCH_3), 3.48 (dd, 1H, $J_{5,6a} = 4.9$ Hz, $J_{6a,6b} = 11.6$ Hz, H-6a), 3.57 (ddd, 1H, H-5), 3.65 (dd, 1H, $J_{5,6b} = 10.3$ Hz, H-6b), 3.93 (broad, d, 1H, valyl α-CH), 4.08 (q, 1H, alanyl-CH), 4.73 (NH), 4.78 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-2), 4.88 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.25 (dd, 1H, $J_{3,4} = 9.1$ Hz, H-3), 5.68 (NH).

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Anal. Calcd for $C_{15}H_{30}Cl_2N_2O_8$ 1/2H_2O (446.32); C, 40.36; H, 7.00; N, 6.28%. Found; C, 40.15; H, 7.21; N, 6.01%.

Methyl 4,6-di-*O*-benzoyl-2-*O*-(*N*-benzoyl-L-alanyl)-3-*O*-(*N*-benzoyl-L-valyl)-α-D-glucopyranoside (9). Compound **8** (86 mg, 0.19 mmol) was treated with benzoyl chloride in pyridine to yield crystalline **9** (53 mg, 35%): mp 181–183 °C (from EtOH-hexane); $[\alpha]_D^{25}$ +55.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.68 and 0.71 (2×d, each 3H, J = 6.7 Hz, 2×valyl-CH_3), 1.52 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 1.99 (m, 1H, valyl-β-CH), 3.49 (s, 3H, 1-OCH_3), 4.32 (ddd, 1H, H-5), 4.42 (dd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.53 (dd, 1H, $J_{5,6b}$ = 3.0 Hz, H-6b), 4.56 (dd, 1H, $J_{\alpha\text{-CH},\beta\text{-CH}}$ = 6.2 Hz, $J_{\alpha\text{-CH,NH}}$ = 9.2 Hz, valyl-α-CH), 4.92 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.98 (q, 1H, J = 7.3 Hz, alanyl-CH), 5.16 (dd, 1H, $J_{2,3}$ = 9.8 Hz H-2), 5.50 (t, 1H, $J_{3,4}$ = 9.8Hz, H-3), 5.84 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 6.34 (d, 1H, valyl-NH), 7.27 (d, 1H, alanyl-NH), 7.28–8.01 (20H, 4×Ph).

Anal. Calcd for $C_{43}H_{44}N_2O_{12}$ 1/2H_2O (789.83); C, 65.39; H, 5.74; N, 3.55%. Found; C, 65.54; H, 5.66; N, 3.48%.

Methyl 4,6-*O*-benzylidene-3-*O*-(*N*-*t*-butoxycarbonyl-D-alanyl)-2-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-α-D-glucopyranoside (10). Compound **1** (2.5 g, 5.5 mmol) was acylated as described for the synthesis of **7** to furnish **10** (2.72 g, 78%): mp 109–111°C; (from EtOAc-petroleum ether); $[\alpha]_D^{21}$ + 17.9° (*c* 1.0, chloroform); IR (KBr) 3421 (NH), 1757, 1714 (ester), 1628, 1504 cm^{-1} (carbamate); ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.34 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 1.41 and 1.44 (2×s, each 9H, 2×*t*-butyl), 3.43 (s, 3H, 1-OCH_3), 3.69 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 3.78 (t, 1H, $J_{5,6a}$ = $J_{6a,6b}$ = 9.8 Hz, H-6a), 3.93 (dt, 1H, $J_{5,6b}$ = 4.9 Hz, H-5), 4.26 and 4.39 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 4.31 (dd, 1H, H-6b), 4.92 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 5.01 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.51 (s, 1H, Ph-CH), 5.61 (t, 1H, H-3), 7.33–7.41 (m, 5H, Ph).

Anal. Calcd for $C_{30}H_{44}N_2O_{12}$ 1/2H_2O (633.69); C, 56.86; H, 7.16; N, 4.42%. Found; C,56.46; H, 7.38; N, 4.29%.

Methyl 3-*O*-(D-alanyl)-2-*O*-(L-alanyl)-α-D-glucopyranoside dihydrochloride (11). Compound **10** (1.5 g, 2.4 mmol) was hydrolyzed as described for the synthesis of **2** to furnish **11** (722 mg, 69%) as an amorphous powder: $[\alpha]_D^{21}$ + 65.2° (*c* 1.0, methanol); IR (KBr) 3403 and 2943 (NH, OH), 1753 (ester), 1593 cm^{-1} (NH); ^{1}H NMR (D_2O) δ 1.38 and 1.45 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.30 (s, 3H, 1-OCH_3), 3.64 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 3.64–3.68 (m, 1H, H-5), 3.68 (dd, 1H, $J_{5,6a}$ = 6.1 Hz, H-6a), 3.76 (dd, 1H, $J_{5,6b}$ = 1.8 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6b), 4.10 and 4.13 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 4.97 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.00 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.27 (t, 1H, H-3).

Anal. Calcd for $C_{13}H_{26}N_2O_8Cl_2$ 3/2H_2O (436.28); C, 35.79; H, 6.70; N, 6.42%. Found; C, 35.78; H, 7.12; N, 6.51%.

Methyl 4,6-di-*O*-benzoyl-3-*O*-(*N*-benzoyl-D-alanyl)-2-*O*-(*N*-benzoyl-L-alanyl)-α-D-glucopyranoside (12). Compound **11** (510 mg, 1.2 mmol) was benzoylated as described for the synthesis of **3** to furnish **12** (357 mg, 39%) as colorless needles from chloroform-light petroleum: mp 215–216 °C; $[\alpha]_D^{21}$ + 39.9° (*c* 1.0, chloroform); IR (KBr) 3430 (NH), 1747 and 1725 (ester), 1645 and 1533 (amide), 1604 and 1580 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.43 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.50

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(s, 3H, 1-OCH_3), 4.33 (ddd, 1H, $J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 3.1 Hz, H-5), 4.43 (dd, 1H, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.56 (dd, 1H, H-6b), 4.61 and 4.98 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 4.99 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.23 (dd, 1H, $J_{2,3}$ = 9.8 H-2), 5.55 (t, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 5.81 (t, 1H, H-4), 7.35-8.04 (m, 20H, 4×Ph).

Anal. Calcd for $C_{41}H_{40}N_2O_{12}$ 1/2H_2O (761.78); C, 64.63; H, 5.43; N, 3.68%. Found; C, 64.70; H, 5.26; N, 3.61%.

Methyl 4,6-*O*-benzylidene-2-*O*-(*N*-*t*-butoxycarbonyl-D-alanyl)-α-D-glucopyranoside (13). Using *N*-*t*-butoxycarbonyl-D-alanine, **13** was prepared from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (3.0 g, 11 mmol) analogously to the preparation of **2**. The crude product was recrystallized from ethyl acetate-light petroleum to give **13** (2.43 g, 49%) as colorless needles: mp 102–104 °C; $[\alpha]_D^{24}$ + 70.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.39 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 1.43 (s, 9H, *t*-butyl), 3.39 (s, 3H, 1-OCH_3), 3.60 (t, 1H, $J_{3,4}$ = 9.1 Hz, $J_{4,5}$ = 9.8 Hz, H-4), 3.76 (t, 1H, $J_{5,6a}$ = $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.86 (dt, 1H, $J_{5,6b}$ = 4.9 Hz, H-5), 4.21 (t, 1H, H-3), 4.29 (dd, 2H, H-6b and alanyl-CH), 4.88 (broad d, 2H, H-1 and H-2), 5.08 (broad s, 1H, alanyl-NH), 5.55 (s, 1H, Ph-CH), 7.35–7.51 (m, 5H, Ph).

Anal. Calcd for $C_{22}H_{31}NO_9$ (453.48); C, 58.27; H, 6.89; N, 3.09%. Found; C, 58.32; H, 7.26; N, 3.02%.

Methyl 4,6-*O*-benzylidene-2-*O*-(*N*-*t*-butoxycarbonyl-D-alanyl)-3-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-α-D-glucopyranoside (14). Compound **13** (1.5 g, 3.3 mmol) was aminoacylated as described for the synthesis of **1** to furnish **14** (1.66 g, 81%) as colorless needles: mp 155–156 °C (from EtOAc-petroleum ether); $[\alpha]_D^{24}$ + 37.4° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.34 and 1.37 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 1.41 and 1.44 (2×s, each 9H, 2×*t*-butyl), 3.40 (s, 3H, 1-OCH_3), 3.70 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 3.78 (t, 1H, $J_{6a,6b}$ = 10.3 Hz, H-6a), 3.92 (ddd, 1H, $J_{5,6b}$ = 4.9 Hz, H-5). 4.31 (dd, 1H, H-6b), 4.91 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 4.92 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.52 (s, 1H, Ph-CH), 5.62 (t, 1H, H-3), 7.33–7.45 (m, 5H, Ph).

Anal. Calcd for $C_{30}H_{44}N_2O_{12}$ (624.68); C, 57.68; H, 7.10; N, 4.48%. Found; C, 57.84; H, 7.21; N, 4.54%.

Methyl 2-*O*-(D-alanyl)-3-*O*-(L-alanyl)-α-D-glucopyranoside dihydrochloride (15). Compound **14** (1.4 g, 2.2 mmol) was hydrolyzed as described for the synthesis of **2** to furnish **15** (385 mg, 43%) as an amorphous powder: $[\alpha]_D^{24}$ + 33.5° (*c* 1.0, methanol); ^{1}H NMR (DMSO-d_6) δ 1.40 (d, 3H, J = 6.7 Hz, alanyl-CH_3), 1.42 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 3.32 (s, 3H, 1-OCH_3), 3.53–3.59 (m, 1H, H-5), 3.55 (dd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6a), 3.59 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 3.62 (dd, 1H, H-6b), 4.13 (broad t, 2H, 2×alanyl-CH), 4.74 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 4.88 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.18 (t, 1H, H-3).

Anal. Calcd for $C_{13}H_{26}N_2O_8$ 2H_2O (409.26); C, 35.06; H, 6.79; N, 6.29%. Found; C, 34.97; H, 7.18; N, 6.20%.

Methyl 4,6-di-*O*-benzoyl-2-*O*-(*N*-benzoyl-D-alanyl)-3-*O*-(*N*-benzoyl-L-alanyl)-α-D-glucopyranoside (16). Compound **15** (392 mg, 0.51 mmol) was benzoylated as described for the synthesis of **3** to furnish **16** (322 mg, 82%) as colorless needles: mp 83–85 °C (from petroleum ether); $[\alpha]_D^{24}$ + 48.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ

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1.21 and 1.49 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.43 (s, 3H, 1-OCH_3), 4.4–4.4 (m, 1H, $J_{4,5}$ = 9.8 Hz, H-5), 4.42 (dd, 1H, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.44 and 4.99 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 4.52 (dd, 1H, $J_{5,6b}$ = 3.1 Hz, H-6b), 4.97 (dd, 1H, $J_{1,2}$ = 3.7 Hz, H-2), 4.98 (d, 1H, H-1), 5.44 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.8 Hz, H-3), 5.81 (t, 1H, H-4), 7.38–8.01 (m, 20H, 4×Ph).

Anal. Calcd for $C_{41}H_{40}N_2O_{12}$ 1/2H_2O (761.77); C, 64.65; H, 5.42; N, 3.68%. Found; C, 64.34; H, 5.61; N, 3.47%.

Methyl 4,6-*O*-benzylidene-2,3-di-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-β-D-glucopyranoside (17). Compound **17** was prepared from methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (5 g, 18 mmol) and *N*-Boc-L-alanine using EDCI as a coupling agent in the presence of DMAP. Yield (8.0 g, 71%), as colorless needles. mp 158–159 °C (from petroleum ether); $[\alpha]_D^{23}$ −54.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.34 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 1.40 and 1.55 (2×s, each 9H, 2×*t*-butyl), 3.52 (s, 3H, 1-OCH_3), 3.74 (dd, 1H, $J_{3,4}$ = 9.8 Hz, $J_{4,5}$ = 9.3 Hz, H-4), 3.82 (t, 1H, $J_{5,6a} = J_{6a,6b}$ = 10.3 Hz, H-6a), 4.35 (2q, 2H, J = 7.3 Hz, 2×alanyl-CH), 4.40 (dd, 1H, $J_{5,6b}$ = 4.9 Hz, H-6b), 4.53 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 5.06 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 5.40 (dd, 1H, H-3), 5.52 (s, 1H, Ph-CH), 7.3–7.5 (5H, Ph).

Anal. Calcd for $C_{30}H_{44}N_2O_{12}$ (624.68); C, 57.68; H, 7.10; N, 4.48%. Found; C, 57.98; H, 7.28; N, 4.59%.

Methyl 2,3-di-*O*-(L-alanyl)-β-D-glucopyranoside dihydrochloride (18). Compound **17** (2.0 g, 3.2 mmol) was hydrolyzed as described for the synthesis of **2** to furnish **18** (830 mg, 61%) as an amorphous powder: $[\alpha]_D^{23}$ −21.3° (*c* 1.0, methanol); ^{1}H NMR (D_2O) δ 1.40 and 1.44 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.43 (s, 3H, 1-OCH_3), 3.54 (ddd, 1H, $J_{4,5}$ = 9.3 Hz, H-5), 3.64 (dd, 1H, H-6a), 3.68 (t, 1H, $J_{3,4}$ = 9.3 Hz, H-4), 3.84 (dd, 1H, $J_{5,6b}$ = 1.5 Hz, H-6b), 4.18 (2q, 2H, J = 7.3 Hz, 2×alanyl-CH), 4.66 (dd, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.92 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 5.25 (t, 1H, H-3).

Anal. Calcd for $C_{13}H_{26}C_{l2}N_2O_8$ H_2O (427.28); C, 36.54; H, 6.60; N, 6.56%. Found; C, 36.37; H, 6.78; N, 6.39%.

Methyl 4,6-di-*O*-benzoyl-2,3-di-*O*-(*N*-benzoyl-L-alanyl)-β-D-glucopyranoside (19). Compound **18** (200 mg, 0.5 mmol) was benzoylated as described for the synthesis of **3** to furnish **19** (180 mg, 50%) as colorless needles (from EtOH): mp 194 °C (dec.); $[\alpha]_D^{23}$ −13.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.22 and 1.52 (2×t, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.52 (s, 3H, 1-OCH_3), 4.04 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, H-5), 4.46 (dd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.58 (dd, 1H, $J_{5,6b}$ = 3.1 Hz, H-6b), 4.59 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.66 and 4.97 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 5.18 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 5.49 (t, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 5.58 (t, 1H, H-4), 7.23–7.99 (20H, 4×Ph).

Anal. Calcd for $C_{41}H_{40}N_2O_{12}$ 1/2H_2O (761.78); C, 64.64; H, 5.43; N, 3.68%. Found; C, 64.68; H, 5.74; N, 3.49%.

Isopropyl 2,3-di-*O*-(*N*-*t*-butoxycarbonyl-L-alanyl)-4,6-*O*-benzylidene-α-D-glucopyranoside (20). Compound **20** was prepared from isopropyl 4,6-*O*-benzylidene-α-D-glucopyranoside (1.5 g, 4.8 mmol) derived from isopropyl α-D-glucopyranoside, and *N*-Boc-L-alanine using EDCI as a coupling agent in the presence of DMAP. The crude product was recrystallized from ethyl acetate to give **20** (2.55 g, 81%) as colorless

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needles: mp 158–160 °C; $[\alpha]_D^{29}$ +38.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.13 and 1.25 (2×d, each 3H, J = 6.1 Hz, 2×isopropyl-CH_3), 1.33 and 1.36 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 1.42 and 1.45 (2×s, each 9H, 2×*t*-butyl), 3.69 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 3.76 (t, 1H, $J_{6a,6b} = 10.4$ Hz, H-6a), 3.85 (m, 1H, J = 6.1 Hz, isopropyl-CH), 4.03 (dt, 1H, $J_{5,6b} = 4.9$ Hz, H-5), 4.29 (dd, 1H, H-6b), 4.35 (broad t, 2H, 2×alanyl-CH), 4.87 (dd, 1H, H-2), 5.17 (d, 1H, H-1), 5.52 (s, 1H, Ph-CH), 5.64 (t, 1H, H-3), 7.33–7.46 (m, 5H, Ph).

Anal. Calcd for $C_{32}H_{48}N_2O_{12}$ (652.74); C, 58.88; H, 7.41; N, 4.29%. Found; C, 58.65; H, 7.77; N, 4.21%.

Isopropyl 2,3-di-*O*-(L-alanyl)-α-D-glucopyranoside dihydrochloride (21). Compound **20** (1.5 g, 2.3 mmol) was hydrolyzed as described for the synthesis of **2** to furnish **21** (540 mg, 64%) as an amorphous powder: $[\alpha]_D^{25}$+35.2° (*c* 1.0, water); ^{1}H NMR (D_2O) δ 1.08 (d, 3H, J = 6.1 Hz, isopropyl-CH_3), 1.19 (d, 3H, J = 6.7 Hz, isopropyl-CH_3), 1.46 and 1.48 (2×d, each 3H, J = 7.3 Hz, 2×alanyl-CH_3), 3.72 (t, 1H, $J_{3,4} = 9.1$ Hz, $J_{4,5} = 9.8$ Hz, H-4), 3.73 (dd, 1H, $J_{6a,6b} = 12.8$ Hz, H-6a), 3.79 (dd, 1H, $J_{5,6b} = 2.4$ Hz, H-6b), 3.81 (dt, 1H, H-5), 3.96 (q, 1H, J = 6.1 Hz, isopropyl-CH), 4.17 and 4.23 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 5.04 (dd, 1H, $J_{2,3} = 10.4$ Hz, H-2), 5.26 (d, 1H, $J_{1,2} = 4.3$ Hz, H-1), 5.37 (t, 1H, H-3); MS m/z 364.18.

Isopropyl 2,3-di-*O*-(*N*-benzoyl-L-alanyl)-4,6-di-*O*-benzoyl-α-D-glucopyranoside (22). Benzoylation of **21** (611 mg, 1.7 mmol) with pyridine and benzoyl chloride afforded **20** (660 mg, 50%) as colorless needles: mp 142–144 °C (from diethyl ether); $[\alpha]_D^{27}$+42.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.19 (d, 3H, J = 6.3 Hz, isopropyl-CH_3), 1.20 (d, 3H, J = 6.1 Hz, isopropyl-CH_3), 1.31 (d, 3H, J = 6.1 Hz, alanyl-CH_3), 1.52 (d, 3H, J = 7.3 Hz, alanyl-CH_3), 3.94 (m, 1H, J = 6.1 Hz, isopropyl-CH), 4.42 (dd, 1H, $J_{5,6a} = 4.9$ Hz, $J_{6a,6b} = 11.6$ Hz, H-6a), 4.46 (dt, 1H, $J_{4,5} = 9.8$ Hz, H-5), 4.53 (dd, 1H, H-6b), 4.63 and 4.93 (2×q, each 1H, J = 7.3 Hz, 2×alanyl-CH), 5.11 (dd, 1H, $J_{2,3} = 9.8$ Hz, H-2), 5.15 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.45 (t, 1H, $J_{3,4} = 9.7$ Hz, H-4), 5.82 (t, 1H, H-3), 7.32–8.01 (m, 20H, 4×Ph).

Anal. Calcd for $C_{43}H_{44}N_{20}O_{12}$ (780.83); C, 66.14; H, 5.68; N, 3.591%. Found: C, 66.31; H, 5.65; N, 3.78%.

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13. As a preliminary result, methyl 3,4-di-*O*-(L-alanyl)-α-D-glucopyranoside, mp 170 °C (dec.); $[\alpha]_D 25 + 121°$ (c 1.0, water), derived from methyl 2-*O*-benzoyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside[11] (8.5%, in 7 steps reactions), was not sweet.

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