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Note

An approach to pseudo-glycopeptides from 2-carbamoyl-2-deoxyglycosides

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Recently, a number of hydrophobic, biologically active oligopeptides, such as the enkephalin analogue Tyr-Gly-Gly-Phe-Leu/Met [1] and the antibacterial tripeptide Leu-Val-Gly-CHN_2 [2], have been synthesized. Coupling of such peptides with sugar units should increase their hydrophilicity and enable easier transport through cytoplasmic membranes [3].

Some years ago, we described the synthesis of methyl 2-*C*-carbamoyl-2-deoxyglycopyranosides (**1**) [4,5] by addition of tosyl isocyanate to glycals, followed by alcoholysis of the unstable [2 + 2]cycloadduct. These are branched monosaccharides structurally related to 2-acetamido-2-deoxy sugars, and have been utilized for further syntheses [5–7]. The carbamoyl function at C-2 in **1** can be employed to link a peptide with the sugar unit, and in this paper we report several possible routes leading to pseudo-glycopeptides from compounds **2** and **3** of the β-D-*gluco* and β-D-*galacto* configurations.

Alkylation of **2** and **3** with *tert*-butyl bromoacetate gave **4** and **5** in 78–80% yield. Prolongation of the reaction time led to formation of a mixture of unidentified compounds containing additional *tert*-butoxycarbonylmethyl substituents but not a tosyl substituent. The tosyl substituent could be removed easily from **4** and **5** by sodium naphthalene reduction to afford **6** and **7**, respectively; benzyl ether groups were unaffected under these conditions. Alkylation of the glycosides **8** and **9**, readily available from **2** and **3**, led to formation of the corresponding *N*-disubstituted compounds **10** and **11** in 70–80% yield.

Esters **6** and **7** were deprotected to give the free acids **12** and **13**, which were in turn coupled with the methyl esters of glycine or L-leucine to afford compounds **14–16**, respectively.

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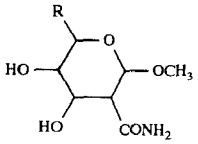


1: R=H, CH_3, CH_2OH

Saponification of **2** and **3** to the free acids failed. Refluxing of **2** in a potassium hydroxide–water–methanol solution for 4 days did not affect the imide function. The free acid could, however, be obtained, via a two-step procedure. Treatment of **2** with phosgene in *N,N*-dimethylformamide, followed by hydrolysis, gave free acid **17** in 30% yield. Acid **17** could be coupled with the methyl ester of glycine to give compound **18**.

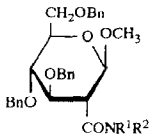
The carbamoyl function in **8** could be activated by its transformation into acyl isocyanate **19**. The isocyanate **19** coupled directly with esters of glycine and leucine, to afford the corresponding ureides **20** and **21**.

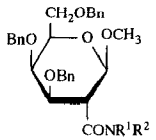
Compounds **14–16**, **18**, and **21** were debenzylated by hydrogenolysis over palladium catalyst, to afford *N*-substituted 2-*C*-carbamoylglycosides **22–25**, respectively.

1. Experimental

All melting points were uncorrected. Optical rotations were measured using a Jasco DIP-360 digital polarimeter. IR spectra were recorded with a Beckman 4240 spectrophotometer. The ^1H NMR and ^{13}C NMR spectra were recorded with Varian Gemini 200 and Bruker AM 500 spectrometers. Column chromatography was performed on Merck Kieselgel 60 (230–400 mesh).

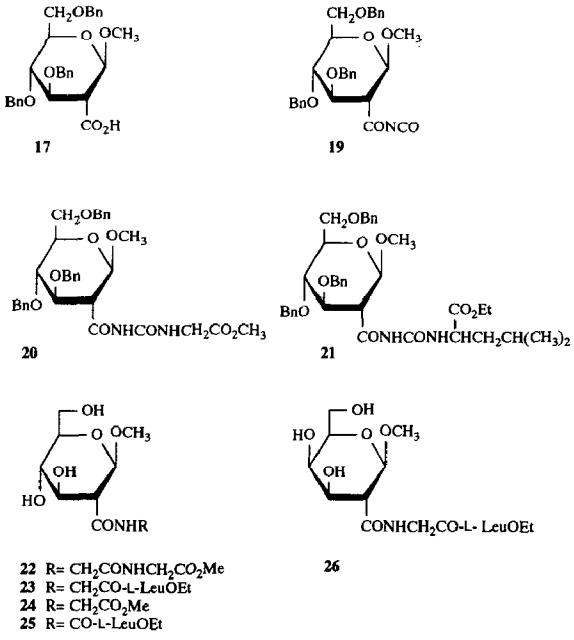
*Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(tosylcarbamoyl)-β-*D*-glucopyranoside* (**2**), *methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(tosylcarbamoyl)-β-*D*-galactopyranoside* (**3**), *methyl 3,4,6-tri-*O*-benzyl-2-*C*-carbamoyl-2-deoxy-β-*D*-glucopyranoside* (**8**), *and*





2 R^1=H, R^2=Ts
4 R^1=CH_2CO_2t-Bu, R^2=Ts
6 R^1=CH_2CO_2t-Bu, R^2=H
8 R^1=R^2=H
10 R^1=R^2=CH_2CO_2t-Bu
12 R^1=CH_2CO_2H, R^2=H
14 R^1=$CH_2CONHCH_2CO_2Me$, R^2=H
15 R^1=CH_2CO-L-LeuOEt, R^2=H,
18 R^1=CH_2CO_2Me, R^2=H

3 R^1=H, R^2=Ts
5 R^1=CH_2CO_2t-Bu, R^2=Ts
7 R^1=CH_2CO_2t-Bu, R^2=H
9 R^1=R^2=H
11 R^1=R^2=CH_2CO_2t-Bu
13 R^1=CH_2CO_2H, R^2=H
16 R^1=CH_2CO-L-LeuOEt, R^2=H



*methyl 3,4,6-tri-*O*-benzyl-2-*C*-carbamoyl-2-deoxy-β-*D*-galactopyranoside* (**9**).—These were obtained according to the procedure described earlier [5].

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-(*N*-tert-butoxycarbonylmethyl-*N*-tosylcarbamoyl)-2-deoxy-β-*D*-glucopyranoside* (**4**).—To a solution of the glycoside **2** (2 g, 3.1 mmol) in benzene were added KOH (9.0 g) and tetrabutylammonium bromide (0.2 g) with vigorous stirring. Subsequently *tert*-butyl bromoacetate (8.0 g, 54 mmol) was added in two portions. The mixture was stirred for 4 h at room temperature, then filtered, washed with water (3 × 15 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product **4** was purified by chromatography (5:1 hexane–EtOAc) to give a colourless oil (1.88 g, 80%); $[\alpha]_D^{24}$ +5.64° (*c* 1.4, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 1760 (C=O ester) and 1700 cm^{-1} (C=O amide). Selected ^1H NMR data (toluene, 363 K): δ 1.37 (s, 9 H, *t*-Bu), 1.95 [s, 3 H, CH_3 (Ts)], 3.18 (s, 3 H, OMe), 3.33 (m, 1 H, H-5), ~3.5 (bs, 1 H, H-2), 3.57 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.62 (dd, 1 H, $J_{5,6a}$ 2.3, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.64 (dd, 1 H, $J_{5,6b}$ 4.4 Hz, H-6b), 4.09 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.0 Hz, H-3), and 4.38 (d, 1 H, H-1). Anal. Calcd for $C_{42}H_{49}NO_{10}S$: C, 66.38; H, 6.50; N, 1.84. Found: C, 66.27; H, 6.85; N, 2.05.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-(*N*-tert-butoxycarbonylmethyl-*N*-tosylcarbamoyl)-2-deoxy-β-*D*-galactopyranoside* (**5**).—Compound **5** was obtained from **3** according to the procedure described above for **4**; 70% yield; syrup; $[\alpha]_D^{24}$ +15.4° (*c* 1.3, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 1760 (C=O ester) and 1700 cm^{-1} (C=O amide). Selected ^1H NMR data (toluene, 363 K): δ 1.35 (s, 9 H, *t*-Bu), 1.94 [s, 3 H, CH_3 (Ts)], 3.16 (s, 3 H, OMe), 3.39 (m, 2 H, H-2,5), 3.55 (dd, 1 H, $J_{6a,6b}$ 9.8, $J_{5,6a}$ 5.6 Hz, H-6a), 3.70 (m, 2 H, H-3,4), 3.78 (m, 1 H, H-6b), 4.24–4.36 (m, 5 H, H-1, NCH_2, CH_2Ph), 4.50, 4.88

(2 d, 2 H, CH_2Ph), 4.71 (s, 2 H, CH_2Ph). Anal. Calcd for $C_{42}H_{49}NO_{10}S$: C, 66.38; H, 6.50; N, 1.84. Found: C, 66.27; H, 6.85; N, 2.05.

Removal of tosyl group.—A solution of naphthalene (1.66 g, 13 mmol) and sodium (0.34 g) in dry 1,2-dimethoxyethane (18 mL) was stirred for 30 min at room temperature. The mixture was cooled to −30°C, and the solution of glycoside **2–5** (2.2 mmol) in 1,2-dimethoxyethane (3 mL) was added. Stirring and cooling were continued for an additional 20 min, then water was added dropwise until the dark green colour disappeared. The organic layer was separated and the water solution was extracted with EtOAc (3 × 15 mL). The combined extracts were dried ($MgSO_4$), then concentrated in vacuo, and the residue was purified by column chromatography. The following compounds were prepared in this manner.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-(*N*-tert-butoxycarbonylmethylcarbamoyl)-2-deoxy-β-*D*-glucopyranoside* (**6**).—Prepared from *N*-tosyl compound **4** in 70% yield; syrup; $[\alpha]_D^{24}$ −8.0° (*c* 1.1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3330 (N–H), 1760 (C=O ester), and 1670 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 1.47 (s, 9 H, *t*-Bu), 2.45 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.6 Hz, H-2), 3.49 (s, 3 H, OMe), 3.50 (m, 1 H, H-5), 3.62 (t, 1 H, $J_{3,4}$ 8.9, $J_{4,5}$ 9.8 Hz, H-4), 3.72 (dd, 1 H, $J_{5,6a}$ 4.1, $J_{6a,6b}$ 10.8 Hz, H-6a), 3.75 (dd, 1 H, $J_{5,6b}$ 2.4 Hz, H-6b), 3.89 (dd, 1 H, *J* 5.9, *J* 18.4 Hz, NCH_AH_B), 3.93 (dd, 1 H, *J* 4.7 Hz, NCH_AH_B), 4.06 (dd, 1 H, H-3), 4.53 (d, 1 H, H-1), and 6.22 (t, 1 H, NH). Anal. Calcd for $C_{35}H_{43}NO_8$: C, 69.40; H, 7.16; N, 2.31. Found: C, 68.60; H, 7.29; N, 2.54.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-(*N*-tert-butoxycarbonylmethylcarbamoyl)-2-deoxy-β-*D*-galactopyranoside* (**7**).—Prepared from *N*-tosyl compound **3** in 60% yield; syrup; $[\alpha]_D^{20}$ +4.22° (*c* 1.1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3340 (N–H), 1750 (C=O ester), and 1660 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 1.47 (s, 9 H, *t*-Bu), 2.83 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 11.0 Hz, H-2), 3.48 (s, 3 H, OMe), 3.57 (m, 1 H, H-5), 3.61 (m, 2 H, H-6a,6b), 3.85 (bd, 1 H, H-4), 3.90 (dd, 1 H, $J_{3,4}$ 2.7 Hz, H-3), 3.94 (m, 2 H, NCH_2), and 4.51 (d, 1 H, H-1). Anal. Calcd for $C_{35}H_{43}NO_8$: C, 69.40; H, 7.16; N, 2.31. Found: C, 68.49; H, 7.29; N, 2.30.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-[*N*,*N*-di-(tert-butoxycarbonylmethyl)carbamoyl]-2-deoxy-β-*D*-glucopyranoside* (**10**).—Prepared from **8**, according to the method described for **4**; reaction time, 24 h; 80% yield; syrup; $[\alpha]_D^{24}$ −15.4° (*c* 1.3, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 1750 (C=O ester) and 1660 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 1.46 (s, 18 H, 2 *t*-Bu), 3.00 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.1 Hz, H-2), 3.46 (s, 3 H, OMe), 3.51 (m, 1 H, H-5), 3.63 (t, 1 H, $J_{4,5}$ 9.8, $J_{3,4}$ 8.6 Hz, H-4), 3.73 (m, 2 H, H-6a,6b), 4.02 (d, 2 H, *J* 17.2 Hz, NCH_AH_B), 4.17 (dd, 1 H, H-3), 4.22 (d, 1 H, NCH_AH_B), 4.24 (d, 2 H, NCH'_2), and 4.52 (d, 1 H, H-1); ^{15}N NMR ($CDCl_3$): δ 255. Anal. Calcd for $C_{41}H_{53}NO_{10}$: C, 68.41: H, 7.42; N, 1.95. Found C, 68.39; H, 7.35; N, 1.88.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-[*N*,*N*-di-(tert-butoxycarbonylmethyl)carbamoyl]-2-deoxy-β-*D*-galactopyranoside* (**11**).—Prepared from **9** by the procedure described above; reaction time, 24 h; 75% yield; syrup; $[\alpha]_D^{24}$ −7.0° (*c* 1.1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 1750 (C=O ester) and 1650 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 1.39 (s, 9 H, *t*-Bu), 1.46 (s, 9 H, *t*-Bu'), 3.33 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 10.7 Hz, H-2), 3.38 (s, 3 H, OMe), 3.58 (m, 3 H, H-5,6a,6b), 3.63 (m, 1 H, H-4), 3.96 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-3), 4.11, 4.16 (2 d, 2 H, NCH_2), 4.22, 4.31 (2 d, 2 H, NCH'_2), and 4.47 (d,

1 H, H-1). Anal. Calcd for $C_{41}H_{53}NO_{10}$: C, 68.41; H, 7.40; N, 1.95. Found: C, 68.25; H, 7.63; N, 1.80.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-[*N*-(carboxymethyl)carbamoyl]-2-deoxy-β-*D*-glucopyranoside* (**12**).—Glycoside **6** (0.80 g, 1.3 mmol) dissolved in a mixture of CH_2Cl_2 (15 mL) and CF_3CO_2H (8 mL) was left for 1.5 h at room temperature. After this time, the mixture was washed with water, until the acid was removed, dried ($MgSO_4$), and concentrated in vacuo. The crude product was used for the next step without purification.

*Methyl 3,4,6-tri-*O*-benzyl-2-*C*-[*N*-(carboxymethyl)carbamoyl]-2-deoxy-β-*D*-galactopyranoside* (**13**).—Compound **13** was prepared from **7**, according to the procedure described for **12**. The product **13** was used for the next step without purification.

*N-[(Methyl 3,4,6,-tri-*O*-benzyl-2-deoxy-β-*D*-glucopyranosid-2-yl)carbonyl]glycylglycine methyl ester* (**14**).—To the ice-cooled solution of H-Gly-OMe · HCl (0.08 g, 0.7 mmol) in CH_2Cl_2 (1.5 mL) were added Et_3N (0.10 mL, 0.7 mmol), glycoside **12** (0.40 g, 0.7 mmol), 1-hydroxybenzotriazole (0.10 g, 0.7 mmol), and dicyclohexylcarbodiimide (0.14 g, 0.1 mmol) with vigorous stirring. The mixture was stirred overnight at room temperature, then filtered, and concentrated in vacuo. The residue was purified by column chromatography (1:2 hexane–EtOAc) to afford **14** (0.29 g, 67%) as a solid; $[\alpha]_D^{24}$ +1.9° (*c* 0.8, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3280 (N–H), 1760 (C=O ester), and 1640 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 2.48 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.7 Hz, H-2), 3.49 (s, 3 H, OMe), 3.51 (dt, 1 H, H-5), 3.65 (t, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.5 Hz, H-4), 3.72 (s, 3 H, CO_2Me), 3.75 (m, 2 H, H-6a,6b), 3.86 (m, 3 H, NCH_2, NCH_AH_B), 4.10 (t, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 4.11 (dd, 1 H, NCH_AH_B), 4.54 (d, 1 H, H-1), 6.32 (t, 1 H, NH), and 6.58 (t, 1 H, NH′). Anal. Calcd for $C_{34}H_{40}N_2O_9$: C, 65.79; H, 6.50; N, 4.51. Found: C, 65.11; H, 6.71; N, 4.10.

*N-[(Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-glucopyranosid-2-yl)carbonyl]glycyl-*L*-leucine ethyl ester* (**15**).—To the ice-cooled solution of H-Leu-OEt · HCl (0.14 g, 0.7 mmol) in CH_2Cl_2 (2 mL) were added Et_3N (0.1 mL, 0.7 mmol), glycoside **12** (0.40 g, 0.7 mmol), 1-hydroxybenzotriazole (0.10 g, 0.7 mmol), and dicyclohexylcarbodiimide (0.14 g, 0.7 mmol) with vigorous stirring. The mixture was stirred overnight at room temperature, then filtered, concentrated in vacuo, and purified by column chromatography (1.5:1 hexane–EtOAc). Product **15** was obtained as white crystals (0.23 g, 48%); mp 128–129°C; $[\alpha]_D^{24}$ +14.7° (*c* 0.8, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3280 (NH), 1740 (C=O ester), 1660 and 1640 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 0.92 [d, 6 H, 2 CH_3 (Leu)], 1.27 [t, 3 H, CH_3 (OEt)], 2.47 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.6 Hz, H-2), 3.49 (s, 3 H, OMe), 3.51 (m, 1 H, H-5), 3.63 (t, 1 H, $J_{3,4}$ 8.9, $J_{4,5}$ 9.8 Hz, H-4), 3.64 (dd, 1 H, *J* 17.0, *J* 5.0 Hz, NCH_AH_B), 3.74 (m, 2 H, H-6a,6b), 4.08 (dd, 1 H, H-3), 4.18 [q, 2 H, CH_2(OEt)], 4.23 (dd, 1 H, *J* 6.6 Hz, NCH_AH_B), 4.53 (d, 1 H, H-1), 4.57 [m, 1 H, NCH (Leu)], 6.35 (t, 1 H, NH), and 6.39 (d, 1 H, NH′). Anal. Calcd for $C_{39}H_{50}N_2O_9$: C, 67.81; H, 7.30; N, 4.06. Found: C, 67.34; H, 7.31; N, 4.32.

*N-[(Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-galactopyranosid-2-yl)carbonyl]glycyl-*L*-leucine ethyl ester* (**16**).—Prepared from galactoside **13** in the way described for

15; 0.16 g (34%); $[\alpha]_D$ +20.29° (*c* 1.1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3320 (N–H), and 1740 (C=O ester), 1680 and 1660 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 0.92 [dd, 6 H, $2CH_3$ (Leu)], 1.26 [t, 3 H, CH_3 (OEt)], 1.45 [m, 1 H, CH (Leu)], 1.62 [m, 2 H, CH_2 (Leu)], 2.85 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 11.0 Hz, H-2), 3.46 (s, 3 H, OMe), 3.59 (m, 1 H, H-5), 3.61 (m, 3 H, H-5,6a,6b), 3.70 (dd, 1 H, *J* 17.0, *J* 5.2 Hz, NCH_ACH_B), 3.77 (d, 1 H, H-4), 3.93 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-3), 4.16 [q, 2 H, CH_2(OEt)], 4.23 (dd, 1 H, *J* 6.5 Hz, NCH_AH_B), 4.51 (d, 1 H, H-1), 4.63 [m, 1 H, NCH (Leu)], 6.28 (t, 1 H, NH), and 6.44 (d, 1 H, NH′). Anal. Calcd for $C_{39}H_{50}N_2O_9$: C, 67.10; H, 7.30; N, 4.06. Found: C, 67.84; H, 7.25; N, 4.99.

*Methyl 3,4,6-tri-O-benzyl-2-C-carboxy-2-deoxy-β-*D-glucopyranoside (**17**).—To the solution of glycoside **2** (1.00 g, 1.5 mmol) in dry DMF (10 mL) was added phosgene in toluene (4 mL) in two portions. The mixture was heated to 50–55°C for 3 h, then cooled to 0°C, and pyridine (4 mL) was added. The solution was washed with water, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by column chromatography (2.5:1 hexane–EtOAc) to give **17** as a solid (0.23 g, 30%); $[\alpha]_D^{20}$ +3.36° (*c* 0.6, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3000 (OH acid) and 1650 cm^{-1} (C=O). Selected ^1H NMR data ($CDCl_3$): δ 2.73 (dd, 1 H, $J_{1,2}$ 8.5, $J_{2,3}$ 10.9 Hz, H-2), 3.43 (s, 3 H, OMe), 3.45 (m, 1 H, H-5), 3.57 (t, 1 H, $J_{3,4}$ 8.9, $J_{4,5}$ 9.7 Hz, H-4), 3.67 (m, 2 H, H-6a,6b), 3.89 (dd, 1 H, H-3), and 4.44 (d, 1 H, H-1). Anal. Calcd for $C_{29}H_{32}O_7$: C, 70.71; H, 6.54. Found: C, 69.80; H, 6.55.

*Methyl 3,4,6-tri-O-benzyl-2-deoxy-2-C-[*N*-(methoxycarbonylmethyl)carbamoyl]-β-*D*-glucopyranoside* (**18**).—Prepared from glycoside **17** in the way described for **14**; 0.28 mg (61.3%); mp 124–126°C; $[\alpha]_D^{23}$ −5.77° (*c* 1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3440 (N–H), 1760 (C=O ester), and 1680 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 2.47 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.6 Hz, H-2), 3.49 (s, 3 H, OMe), 3.51 (m, 1 H, H-5), 3.62 (t, 1 H, $J_{3,4}$ 8.9, $J_{4,5}$ 9.7 Hz, H-4), 3.73 (s, 3 H, CO_2Me), 3.74 (m, 2 H, H-6a,6b), 4.02 (m, 2 H, NCH_2), 4.07 (dd, 1 H, H-3), 4.52 (d, 1 H, H-1), and 6.24 (t, 1 H, *J* 5.0 Hz, NH). Anal. Calcd for $C_{32}H_{37}NO_8$; C, 68.18; H, 6.61; N, 2.48. Found: C, 68.15; H, 6.76; N, 2.71.

N-*[(Methyl 3,4,6-tri-O-benzyl-2-deoxy-β-*D*-glucopyranosid-2-yl)carbonyl-carbamoyl]glycine methyl ester* (**20**).—To the solution of glycoside **8** (0.5 g, 1 mmol) in dry 1,2-dichloroethylene (5 mL) was added oxyalyl chloride (0.4 mL, 4 mmol) in 1,2-dichloroethylene (0.4 mL). The mixture was refluxed for 3 days, then cooled to room temperature, and Et_3N (0.5 mL) and H-Gly-OMe (0.07 g, 1 mmol) in dry $CHCl_3$ were added. Stirring was continued for 1.5 h, then the solution was washed with water and aq Na_2CO_3, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by column chromatography (2:1 hexane–EtOAc) to afford **20** (0.50 g, 66.6%) as white crystals; mp 163°C; $[\alpha]_D^{20}$ +12.6° (*c* 1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3400 (N–H), 1800 (C=O ester), and 1720 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 2.45 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 10.6 Hz, H-2), 3.48 (m, 1 H, H-5), 3.49 (s, 3 H, OMe), 3.65 (t, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.6 Hz, H-4), 3.74 (m, 2 H, H-6a,6b), 3.77 (s, 3 H, CO_2Me), 4.03 (dd, 1 H, H-3), 4.09 (m, 2 H, NCH_2), 4.48 (s, 1 H, H-1), 7.66 (s, 1 H, NH), and 8.63 (t, 1 H, NH′). Mass spectrum: *m/z*, $M^+ - CH_3OH$. Found: 574.2315. Calcd for $C_{32}H_{34}N_2O_8$: 574.2316.

N-*[(Methyl 3,4,6-tri-O-benzyl-2-deoxy-β-*D*-glucopyranosid-2-yl)carbonylcarba-*

moyl]-L-leucine ethyl ester (**21**).—To the solution of glycoside **8** (0.5 g, 1 mmol) in dry 1,2-dichloroethylene (5 mL) was added oxalyl chloride (0.4 mL, 4 mmol) in 1,2-dichloroethylene (0.4 mL). The mixture was refluxed for 3 days, then cooled to room temperature, and Et_3N (0.5 mL) and H-Leu-OEt (0.12 g, 1 mmol) in dry $CHCl_3$ were added. Stirring was continued for 4 h, then the solution was washed with water and aq Na_2CO_3, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by column chromatography (2:1 hexane–EtOAc) to afford **21** (0.20 g, 30%); mp 114°C; $[\alpha]_D^{20}$ +11.46° (*c* 1, CH_2Cl_2); $\nu_{max}^{CHCl_3}$ 3420 and 3320 (N–H), 1750 (C=O ester), and 1690 cm^{-1} (C=O amide). Selected ^1H NMR data ($CDCl_3$): δ 0.93 [dd, 6 H, 2 CH_3 (Leu)], 1.28 [t, 3 H, CH_3 (OEt)], 1.62 [m, 1 H, CH (Leu)], 1.68 [m, 2 H, CH_2 (Leu)], 2.47 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 10.6 Hz, H-2), 3.48 (m, 1 H, H-5), 3.49 (s, 3 H, OMe), 3.65 (t, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.6 Hz, H-4), 3.74 (m, 2 H, H-6a,6b), 4.04 (dd, 1 H, H-3), 4.21 [m, 2 H, CH_2 (OEt)], 4.48 (d, 1 H, H-1), 4.54 [m, 1 H, NCH (Leu)], 7.66 (s, 1 H, NH), and 8.60 (d, 1 H, NH'). Anal. Calcd for $C_{38}H_{48}N_2O_9$: C, 67.44; H, 7.15; N, 4.14. Found: C, 67.20; H, 7.14; N, 4.26.

Removal of benzyl groups.—To the solution of glycoside (**14–16**, **18**, **21**; 0.1 mmol) in dry MeOH was added a catalytic amount of Pd (10%)/C. The mixture was stirred overnight at room temperature under hydrogen, then filtered, concentrated in vacuo, and purified by column chromatography. The following compounds were prepared in this way.

N-*[(Methyl 2-deoxy-β-D-glucopyranosid-2-yl)carbonyl]glycyl-L-leucine ethyl ester* (**23**).—Prepared from **15**; mp 159–160°C; $[\alpha]_D^{20}$ +33.9° (*c* 1, MeOH); ν_{max}^{MeOH} (film), 1750 (C=O ester), and 1710 and 1660 cm^{-1} (C=O amide). ^1H NMR data (CD_3OD): δ 0.93 [dd, 6 H, 2 CH_3 (Leu)], 1.26 [t, 3 H, CH_3 (OEt)], 1.59 [m, 1 H, CH (Leu)], 1.67 [m, 2 H, CH_2 (Leu)], 2.38 (dd, 1 H, $J_{1,2}$ 8.5, $J_{2,3}$ 10.7 Hz, H-2), 3.30 (m, 2 H, H-4,5), 3.47 (s, 3 H, OMe), 3.71 (m, 1 H, H-6a), 3.78 (m, 1 H, H-3), 3.81 (d, 1 H, *J* 17.0 Hz, NCH_ACH_B), 3.88 (m, 1 H, H-6b), 3.99 (d, 1 H, NCH_ACH_B), 4.16 [m, 2 H, CH_2 (OEt)], 4.49 [dd, 1 H, NCH (Leu)], and 4.54 (d, 1 H, H-1). Anal. Calcd for $C_{18}H_{32}N_2O_9$: C, 51.42; H, 7.67; N, 6.66. Found: C, 51.21; H, 7.67; N, 6.71.

N-*[Methyl 2-deoxy-β-D-galactopyranosid-2-yl)carbonyl]glycyl-L*-leucine ethyl ester (**26**).—Prepared from **16**; syrup; $[\alpha]_D^{20}$ +14.36° (*c* 1, MeOH); ν_{max}^{MeOH} (film) 1760 (C=O ester) and 1670 cm^{-1} (C=O amide). Selected ^1H NMR data (CD_3OD): δ 0.93 [m, 6 H, 2 CH_3 (Leu)], 1.26 [t, 3 H, CH_3 (OEt)], 1.59 [m, 1 H, CH (Leu)], 2.64 (dd, 1 H, $J_{1,2}$ 8.7, $J_{2,3}$ 10.7 Hz, H-2), 3.47 (s, 3 H, OMe), 3.49 (m, 1 H, H-5), 3.78 (m, 4 H, H-4,6a,6b, NCH_AH_B), 3.88 (dd, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.02 (d, 1 H, NCH_ACH_B), 4.16 [m, 2 H, CH_2 (OEt)], 4.49 (d, 1 H, H-1), and 4.49 [m, 1 H, NCH (Leu)]. Anal. Calcd for $C_{18}H_{32}N_2O_9$: C, 51.42; H, 7.67; N, 6.66. Found: C, 51.36; H, 7.81; N, 6.79.

Methyl 2-deoxy-2-C-[N-(methoxycarbonylmethyl)carbamoyl]-β-D-glucopyranoside (**24**).—Prepared from **18**; mp 171–173°C; $[\alpha]_D^{20}$ +13.4° (*c* 0.5, MeOH); ν_{max}^{MeOH} (film) 1750 (C=O ester), 1780 and 1790 cm^{-1} (C=O amide). Selected ^1H NMR data (CD_3OD): δ 2.37 (dd, 1 H, $J_{1,2}$ 8.5, $J_{2,3}$ 10.6 Hz, H-2), 3.27 (m, 2 H, H-4,5), 3.46 (s, 3 H, OMe), 3.70 (m, 1 H, H-6a), 3.72 (s, 3 H, CO_2Me), 3.77 (m, 1 H, H-3), 3.88 (m, 1 H, H-6b), 3.97 (s, 2 H, NCH_2), and 4.50 (d, 1 H, H-1). Anal. Calcd for $C_{11}H_{19}NO_8$: C, 45.05; H, 6.53; N, 4.78. Found: C, 45.83; H, 6.74; N, 3.94.

N-[(Methyl 2-deoxy-β-D-glucopyranosid-2-yl)carbonylcarbamoyl]-L-leucine ethyl ester (**25**).—Prepared from **21**; syrup; $[\alpha]_D^{20}$ −4.5° (*c* 0.35, MeOH); ν_{max}^{MeOH} (film) 1740 (C=O ester), 1700 and 1680 cm^{-1} (C=O amide). Selected ^1H NMR data (CD_3OD): δ 0.96 [dd, 6 H, $2CH_3$ (Leu)], 1.27 [t, 2 H, CH_2 (OEt)], 1.65 [m, 1 H, CH (Leu)], 1.71 [m, 2 H, CH_2 (Leu)], 2.50 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.4 Hz, H-2), 3.27 (m, 2 H, H-4,5), 3.52 (s, 3 H, OMe), 3.70 (m, 1 H, H-6a), 3.78 (dd, 1 H, $J_{3,4}$ 10.7 Hz, H-3), 3.88 (m, 1 H, H-6b), 4.28 [m, 2 H, CH_2 (OEt)], 4.28 [m, 1 H, NCH (Leu)], and 4.52 (d, 1 H, H-1). Mass spectrum: *m/z*, $M^+ - OCH_3$. Found: 375.1768. Calcd for $C_{16}H_{27}N_2O_8$: 375.1767.

N-[(Methyl 2-deoxy-β-D-glucopyranosid-2-yl)carbonyl]glycylglycine methyl ester (**22**).—Prepared from **14**; syrup; $[\alpha]_D^{16}$ −1.8° (*c* 1.3, MeOH); $\nu_{max}^{CHCl_3}$ (film) 3340 (N–H, O–H), 1750 (C=O, ester), and 1660 cm^{-1} (C=O, amide). Selected ^1H NMR data (CD_3OD): δ 2.38 (dd, 1 H, $J_{1,2}$ 8.5, $J_{2,3}$ 10.7 Hz, H-2), ~3.3 (m, 2 H, H-4,5), 3.46 (s, 3 H, OMe), 3.69 (m, 1 H, H-6a), 3.71 (s, 3 H, OMe), 3.77 (m, 1 H, H-3), 3.78 (d, 1 H, *J* 17.0 Hz, NCH_AH_B), 3.87 (m, 1 H, H-6b), 3.93 (2 d, 2 H, *J* 17.7 Hz, NCH_2), 4.04 (d, 1 H, CH_AH_B), and 4.58 (d, 1 H, H-1). Mass spectrum: *m/z*, $M^+ + H$. Found: 351.1390. Calcd for $C_{13}H_{23}N_2O_9$: 351.1391.

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3. References

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