A Serendipitous Discovery of a New *C*-Furanosyl Glycine Synthesis via Thiazole-Based Aminohomologation of Hexopyranoses

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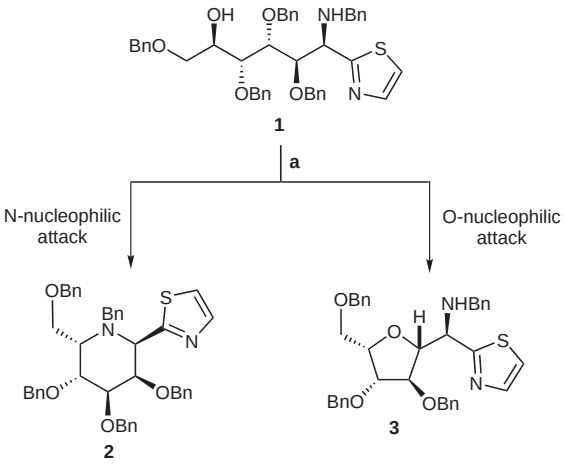
Abstract: Ring closure via microwave-assisted intramolecular OMs displacement by a γ-OBn group (O-nucleophilic attack) in protected polyhydroxylated *N*-Boc-thiazolylalkyl amines afforded *C*-furanosides (37–81%) featuring a chiral thiazolylmethylamino side chain, which, upon thiazole to carboxylate (through aldehyde) transformation, furnished enantiopure *C*-furanosyl glycines.

Key words: amino acids, cyclization, glycopeptides, glycosides, ring closure

The importance of anomerically carbon-linked sugar amino acids, i.e. authentic *C*-glycosyl amino acids, as key building blocks for the post-translational modification of natural glycopeptides is widely recognized.[1] This structural change is known to enhance the stability of glycopeptides toward chemical and enzymatic degradation as well as modulate the conformation and folding with effects on molecular recognition and interactions. Therefore various synthetic routes have been developed in recent years,[2] especially those leading to methylene isosteres of natural *O*-glycosyl α-amino acids, such as L-serine, and L-threonine, and ethylene isosteres of *N*-glycosyl L-asparagines which are the most common components of native glycopeptides.[3] Quite recently attention has been also addressed in our laboratory to the synthesis of *C*-glycosyl β-amino acids[2b,4] since these compounds may serve to introduce a new and quite substantial element of diversity in non-natural *C*-glycosyl amino acid libraries. *C*-Glycosyl glycines featuring the α-amino acid group (glycinyl moiety) directly linked to the sugar fragment have been prepared as well.[2] Search for the synthesis of this special class of sugar amino acids was initially driven by their potential use as building blocks for *C*-nucleoside antibiotics,[5] especially polyoxin and nikkomycin analogues. They are also of great value as components of inhibitors of bacterial synthetases.[6] In recent work *C*-ribosyl glycine derivatives have been employed as platforms for the preparation of various pyrazine *C*-nucleosides serving in a study of hydrogen bonding interactions in DNA and RNA strands.[7] Most of the reported synthetic methods to *C*-glycosyl glycines involve the introduction of a glycinyl group equivalent at the anomeric carbon of a sugar substrate or the construction of the glycinyl moiety by exploiting a carbon-linked functionality already in place in a stereochemically well-defined manner. All methods suffer from various drawbacks such as the scarce stereochemical efficiency, the numerous steps involved, and the lack of generality. Hence the introduction of new synthetic routes to *C*-glycosyl glycines appears to be of great utility. Thus, we would like to report here on a new method that we have discovered in the course of our research on the synthesis of homoazasugars by the thiazole-based aminohomologation of pentafuranoses[8] and hexopyranoses[9] through their open-chain nitrones as intermediates. In the latter investigation[9] we observed that amino alcohol **1**, derived from D-mannose,[10] upon activation as O-mesylate and heating in MeCN afforded both the target piperidine **2** as major product (52%) via intramolecular N-nucleophilic displacement of the OMs group and furanose **3** (30%) via O-nucleophilic attack (Scheme 1).



Scheme 1 *Reagents and conditions*: a) MsCl, Et_3N, TMEDA, anhyd toluene, 0–5 °C, 2 h; then heating in refluxing MeCN.

The stereospecific formation of *C*-furanosides via intramolecular nucleophilic displacement of an activated OH group by a γ-benzyloxy group, was earlier reported by Martin and Yang and their co-workers.[11] However, examples of *C*-furanosides bearing chiral side chains whose substituents were prone to undergo synthetic transformations, were not described. On the other hand, in the light of the amply documented one-pot thiazole-to-formyl transformation and oxidation of the aldehyde to carboxylic acid,[12] compound **3** can be regarded as a potential precursor to an optically pure *C*-furanosyl glycine. This synthetic route was attractive because it overcame the

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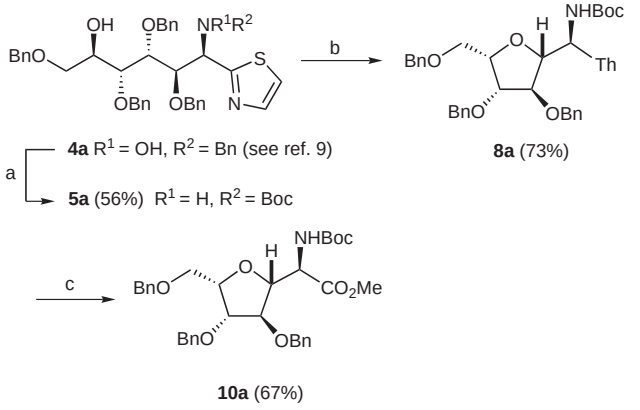
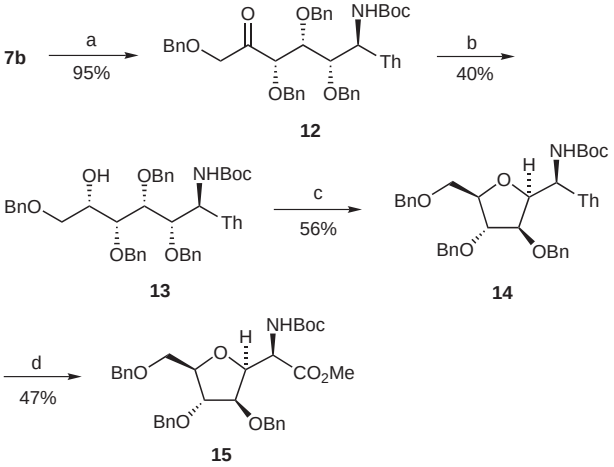
main problem afflicting other approaches to these sugar amino acids, namely the control of the configuration of the anomeric carbon of the sugar moiety as well as the configuration of the asymmetric carbon bearing the amino group in the glycinyl residue.[13] However, in order to optimize the method to a synthetically relevant level, the formation of piperidine **2** via the N-nucleophilic displacement needed to be inhibited. We envisaged achieving this crucial objective by decreasing the nucleophilic power of the nitrogen atom of the amino alcohol. To this aim the transformation of the NHBn group into NHBoc was considered. Hence the *N*-Boc-protected amino alcohol **5a** (Scheme 2) was prepared by reductive dehydroxylation and debenzylation of the N(OH)Bn group[14] of the known thiazolylalkylhydroxylamine **4a** and treatment of the crude amine thus formed with Boc_2O.[15] The mesylation of alcohol **5a** followed by heating the crude material in refluxing MeCN for 12 hours afforded the *C*-furanoside **8a**, still in modest yield (35%), while no piperidine formation was detected as evidenced by NMR analysis. An unsatisfactory result (40% of **8a**) was also obtained under harsher thermal condition (DMF, 150 °C, 12 h). Therefore, given the well established beneficial effects of microwave irradiation on rates and yields of organic reactions,[16] we decided to apply this technique to our system. To our delight microwave heating of the crude mesylate at 150 °C for 20 minutes in DMF (sealed tube) increased the yield of **8a** to the acceptable value of 73%.[17]



Scheme 2 *Reagents and conditions*: a) $TiCl_3$, MeOH, r.t., 15 min; then Boc_2O, $NaHCO_3$, dioxane, r.t., 24 h; b) MsCl, pyridine, 0 °C to r.t., 2 h; then DIPEA, DMF, microwave; c) MeOTf, MeCN, r.t., 15 min; then $NaBH_4$, MeOH, 0 °C to r.t., 15 min; then $CuO/CuCl_2{\cdot}2H_2O$, 10:1 MeCN–H_2O, r.t., 15 min; then $NaClO_2$, H_2O_2, NaH_2PO_4, MeCN, r.t., 2 h; then CH_2N_2, Et_2O, 0 °C.

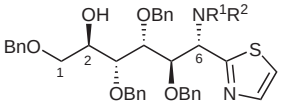
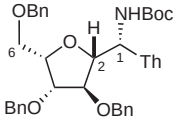
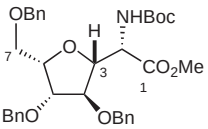
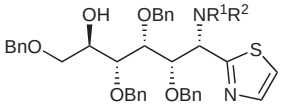
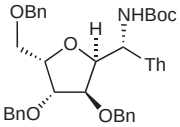
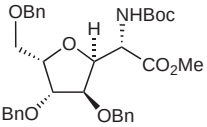
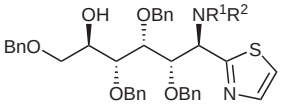
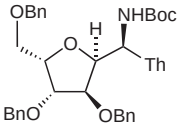
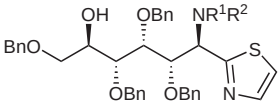
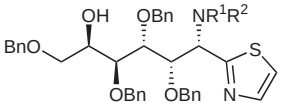
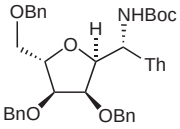
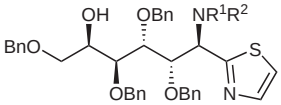
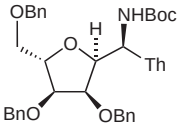
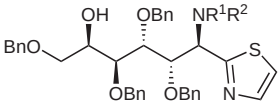
The substitution of the NHBn for the NHBoc group not only favored the O-nucleophilic pathway, but made also the final step readily feasible since the latter group is well known to be tolerated by the thiazole-to-formyl transformation protocol (N-methylation, reduction, hydrolysis) while the former is not.[18] This allowed for the effective elaboration of **8a** into aldehyde which upon oxidation with $NaClO_2$ and treatment with CH_2N_2 afforded *C*-furanosyl glycinate **10a** in very good yield.[19] The structure of both **8a** and **10a** was supported by mono- and bidimensional NMR analysis and ROESY experiments. Given this successful result, the above reaction sequence was extended to alcohol **6a** derived from D-mannose as well and to the pairs of stereoisomers **4b**/**6b** and **4c**/**6c** (Table 1) whose hexopyranose progenitors were D-glucose and D-galactose, respectively.[9] With one exception, i.e. derivative **4c**, these compounds were transformed into the corresponding optically pure *C*-furanosyl glycinates **10b** and **11a–c** in variable yet fair yields.[20] The missing product **8c** from D-galactose was due to the unsuccessful cyclization of *N*-Boc-amino alcohol **5c** to *C*-furanoside **8c** under the standard conditions adopted for the other stereoisomers. This observation together with the exceptionally scarce efficiency registered in the conversion of **7c** to **9c** indicates the high sensitivity of the intramolecular O-nucleophilic substitution process to the structure of the substrate.[21] It is worth noting that the *C*-glycosyl glycines **10** and **11** prepared belong to the L-series of carbohydrates. However, a similar approach starting from L-hexopyranose would lead to the diastereoisomers of the D-series. Nevertheless, we envisaged the approach to this class of compounds by exploiting the C2-epimers of the alcohols employed above. While attempts to epimerize the D-glucose derived amino alcohol **7b** via Mitsunobu reaction [*p*-nitrobenzoic acid, DEAD (diethyl azodicarboxylate), PPh_3, THF, 0 °C] met with failure, the oxidation–reduction sequence earlier applied to similar compounds in our laboratory[22] gave satisfactory results (Scheme 3).



Scheme 3 *Reagents and conditions*: a) Ac_2O, DMSO, r.t., overnight; b) $NaBH_4$, MeOH, 0 °C to r.t., 15 min; c) and d) see Scheme 2.

Hence, **7b** was transformed into ketone **12** via Moffat oxidation and this was reduced by $NaBH_4$ at room temperature to give a mixture of **7b** and the desired epimer **13** in an almost 1:1 ratio.[23] Fortunately these diastereoisomers were easily separable by column chromatography, thus allowing the recycling of **7b** for further epimerization. Finally, derivative **13** underwent the expected O-nucleophilic substitution leading to the *C*-furanoside **14** in fair yield. Thereafter this intermediate was transformed into the target *C*-glycosyl glycinate **15** featuring the D-arabinosyl ring. This result may serve to broaden the

Table 1 Other *C*-Furanosyl Glycines **10** and **11** and their Intermediates Prepared by Aminohomologation of Hexopyranoses

Hexopyranose	Alcohol (yield, %)	*C*-Furanoside (yield, %)[b]	*C*-Furanosyl glycine (yield, %)[b]
D-Mannose			
	6a[a] R^1 = OH, R^2 = Bn **7a** (68)[b] R^1 = H, R^2 = Boc	**9a** (73)	**11a** (34)
D-Glucose			
	4b[a] R^1 = OH, R^2 = Bn **5b** (52)[b] R^1 = H, R^2 = Boc	**8b** (81)	**10b** (61)
D-Glucose			
	6b[a] R^1 = OH, R^2 = Bn **7b** (20)[b] R^1 = H, R^2 = Boc	**9b** (85)	**11b** (67)
D-Galactose			
	4c[a] R^1 = OH, R^2 = Bn **5c** (43)[b] R^1 = H, R^2 = Boc	**8c** (0)	
D-Galactose			
	6c[a] R^1 = OH, R^2 = Bn **7c** (47)[b] R^1 = H, R^2 = Boc	**9c** (37)	**11c** (29)

[a] See ref. 9.
[b] Same reagents and conditions as in Scheme 2.

potential of the method as it allows introducing a new element of diversity in libraries of this class of sugar amino acids.

In conclusion, the unexpected O-nucleophilic substitution reaction occurring in heavily functionalized chiral amino alcohols generated from hexopyranoses has been converted into a stereospecific synthesis of a class of amino acids of a rather difficult access such as enantiopure *C*-furanosyl glycines. It is worth noting that all the amino acids prepared are orthogonally protected building blocks, which are therefore well suited for peptide and nucleoside synthesis.

However, while this synthetic method may suffer for the number of steps, its stereospecificity, the simple yet efficient chemistry involved, and the broad scope, are all favorable features that concur positively to some synthetic utility. For instance a service can be foreseen in the preparation of libraries of special and stereodiversified glycoconjugates for biological testing.

Acknowledgment

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(15) **Typical Procedure for Entry *N*-Boc-Amines 5a–c, 7a–c.** To a stirred solution of *N*-benzyl-*N*-glycosylhydroxylamines **4a**–**c**, **6a**–**c** (0.50 g, 0.69 mmol) in MeOH (9.0 mL) was added a 12% HCl solution of $TiCl_3$ (1.22 mL, 1.71 mmol). Stirring was manteined for an additional 15 min at r.t., then 5 M NaOH was added dropwise until pH 7 (the solution became white). After stirring for an additional 5 min, the primary amine was extracted with EtOAc (3 × 25 mL). The organic phase was washed with brine (2 × 20 mL), dried over Na_2SO_4, and concentrated. Crude primary amine was dissolved in dioxane (6.0 mL) and Boc_2O (330 mg, 1.50 mmol) was added in one portion. Then some drops of a sat. solution of $NaHCO_3$ were added to the mixture until pH 7.5. Stirring was mantained for 18 h, then the reaction was quenched with a 10% citric acid solution (4.0 mL). The protected amine was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL) and H_2O (10 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was eluted from a column of silica gel with the suitable elution system to give the *N*-Boc-protected amines **5a**–**c**,**7a**–**c**. Column chromatography with 3:1 cyclohexane–EtOAc afforded **5a** (278 mg, 56%) as a syrup. $[\alpha]_D$ 5.9 (*c* 0.7, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.78 (d, 1 H, *J* = 3.2 Hz, Th), 7.42–7.00 (m, 21 H, 4 Ph and Th), 5.86 (d, 1 H, $J_{NH,6}$ = 9.0 Hz, NH), 5.59 (dd, 1 H, $J_{6,5}$ = 1.0 Hz, $J_{6,NH}$ = 9.0 Hz, H-6), 4.72 and 4.62 (2 d, 2 H, *J* = 11.0 Hz, C*H*$_2$Ph), 4.72 and 4.59 (2 d, 2 H, *J* = 11.0 Hz, C*H*$_2$Ph), 4.58 (dd, 1 H, $J_{5,4}$ = 8.0 Hz, $J_{5,6}$ = 1.0 Hz, H-5), 4.54 and 4.51 (2 d, 2 H, *J* = 11.0 Hz, C*H*$_2$Ph), 4.23 and 3.99 (2 d, 2 H, *J* = 11.0 Hz, C*H*$_2$Ph), 4.10 (br s, 1 H, H-2), 3.97 (dd, 1 H, $J_{4,3}$ = 3.5 Hz, $J_{4,5}$ = 8.0 Hz, H-4), 3.88 (dd, 1 H, $J_{3,2}$ = 8.0 Hz, $J_{3,4}$ = 3.5 Hz, H-3), 3.72 (dd, 1 H, $J_{1a,1b}$ = 9.5 Hz, $J_{1a,2}$ = 3.0 Hz, H-1a), 3.64 (dd, 1 H, $J_{1b,1a}$ = 9.5 Hz, $J_{1b,2}$ = 5.5 Hz, H-1b), 2.65 (s, 1 H, OH), 1.45 (s, 9 H, *t*-Bu). ^{13}C NMR ($CDCl_3$): δ = 173.9, 155.4, 143.2, 138.5, 138.2, 137.9, 137.5, 128.6, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.5, 127.0, 118.9, 80.9, 80.1, 78.4, 78.1, 74.9, 73.8, 73.4, 72.8, 71.2, 70.0, 60.4, 53.5, 28.3, 21.1, 14.2. MALDI-TOF MS (724.9): *m/z* 747.1 [M + Na], 763.1 [M + K]. Anal. Calcd for $C_{42}H_{48}N_2O_6S$: C, 71.16; H, 6.82; N, 3.95. Found: C, 71.17; H, 6.79; N, 3.97.
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(17) **Typical Procedure for Entry *C*-Furanosides 8a,b, 9a–c, 14.** To a cooled (0 °C), stirred solution of *N*-Boc-protected amines **5a**–**c**, **7a**–**c**, **13** (175 mg, 0.24 mmol) in pyridine (6.0 mL) was added mesyl cloride (56 μL, 0.72 mmol) in one portion. The mixture was stirred for an additional 2 h, then some drops of MeOH were added and the solvent was removed in vacuo. The residue was taken up in EtOAc (10 mL) and washed with a sat. solution of $NaHCO_3$ (2 × 10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. A 0.5–2.0 mL process vial was filled with the above crude mesylated intermediate, DIPEA (83 μL, 0.48 mmol), and anhyd DMF (2.0 mL). The vial was sealed with the Teflon septum and aluminium crimp by using an appropriate crimping tool. The vial was then placed in its correct position in the Biotage Initiator cavity where irradiation for 20 min at 150 °C was performed. After the full irradiation sequence was completed, the vial was cooled to r.t. and then opened. The solution was transferred into a round-bottomed flask and the solvent was removed in vacuo. The residue was taken up in EtOAc (10 mL), and washed with a sat. solution of $NaHCO_3$ (2 × 15 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was eluted from a column of silica gel with the suitable elution system to give the *C*-furanosides **8a**,**b**, **9a**–**c**, **14**. Column chromatography with 3:1 cyclohexane–EtOAc afforded **8a** (112 mg, 73%) as a syrup. $[\alpha]_D$ 42.8 (*c* 1.0, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.52 (d, 1 H, *J* = 3.2 Hz, Th), 7.20–7.00 (m, 15 H, 3 Ph), 6.50 (d, 1 H, *J* = 3.2 Hz, Th), 6.36 (d, 1 H, $J_{NH,2}$ = 7.5 Hz, NH), 5.69 (br s, 1 H, H-2), 4.90 (br s, 1 H, H-3), 4.42 and 4.18 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.26 (s, 2 H, CH_2Ph), 4.21 and 4.14 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.14 (dd, 1 H, $J_{4,3}$ = 1.5 Hz, $J_{4,5}$ = 4.0 Hz, H-4), 4.11 (ddd, 1 H, $J_{6,5}$ = 1.5 Hz, $J_{6,7a}$ = 6.5 Hz, $J_{6,7b}$ = 5.0 Hz, H-6), 3.83 (dd, 1 H, $J_{5,4}$ = 4.0 Hz, $J_{5,6}$ = 1.5 Hz, H-5), 3.66 (dd, 1 H, $J_{7a,6}$ = 6.5 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7), 3.52 (dd, 1 H, $J_{7b,6}$ = 5.0 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b), 1.35 (s, 9 H, *t*-Bu). ^{13}C NMR (C_6D_6): δ = 172.1, 155.6, 142.9, 138.5, 137.9, 128.3, 128.2, 128.1, 127.9, 127.7, 127.4, 118.4, 110.3, 98.2, 85.4, 83.0, 82.4, 80.0, 73.0, 71.6, 71.3, 67.4, 55.3, 35.5, 28.0. MALDI-TOF MS (616.7): *m/z* 655.2 [M + K]. Anal. Calcd for $C_{35}H_{40}N_2O_6S$: C, 68.16; H, 6.54; N, 4.54. Found: C, 68.22; H, 6.60; N, 4.59.
(18) (a) Dondoni, A.; Marra, A.; Perrone, D. *J. Org. Chem.* **1993**, *58*, 275. (b) Dondoni, A.; Perrone, D. *Synthesis* **1993**, 1162. (c) Dondoni, A.; Perrone, D. *Aldrichimica Acta* **1997**, *30*, 35. (d) Dondoni, A. *Synthesis* **1998**, 1681. (e) Dondoni, A.; Marra, A. *Chem. Rev.* **2004**, *5*, 2557.
(19) **Typical Procedure for Entry *C*-Glycosyl Glycines 10a,b, 11a–c, 15.** A mixture of the thiazole derivative **8a**,**b**, **9a**–**c**, **14** (164 mg, 0.26 mmol), activated 4 Å MS (400 mg) and MeCN (4.0 mL) was stirred at r.t. for 10 min then methyl triflate (32 μL, 0.28 mmol) was added in one portion. The suspension was stirred

for an additional 15 min then the solvent was removed under reduced pressure. The residue was taken up in MeOH (4.0 mL), cooled to 0 °C and treated with $NaBH_4$ (22 mg, 0.56 mmol). The mixture was stirred at r.t. for 15 min, diluted with acetone, filtered through a pad of Celite®, and concentrated in vacuo. The residue was taken up in 10:1 MeCN–H_2O (4.0 mL) and then treated with CuO (60 mg, 0.78 mmol), and $CuCl_2 \cdot 2H_2O$ (48 mg, 0.28 mmol). The resulting suspension was stirred at r.t. for 10 min, then filtered through a pad of Celite® and concentrated in vacuo at a temperature below 30 °C. The residue was partitioned between brine (30 mL) and Et_2O (30 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic extracts were washed with sat. aq EDTA (disodium salt), brine, dried over Na_2SO_4, filtered, and concentraed to give the essentially pure α-amino aldehyde which was taken up in MeCN (2 mL). The resulting solution was treated with 35% aq H_2O_2 (40 μL), 1.2 M aq KH_2PO_4 (0.2 mL) and 0.17 M aq $NaClO_2$ (1.4 mL). After 2 h the reaction was acidified with 1 N aq HCl till pH = 2 and the resulting mixture was extracted with EtOAc (3 × 20 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated. The crude carboxylic acid was taken up in Et_2O, the solution was kept at 0 °C and treated with an ethereal solution of CH_2N_2 until a pale yellow colour persisted. The solution was stirred for an additional 15 min, then the residue was dried in vacuo. The residue was eluted from a column of silica gel with the suitable elution system to give the corresponding *C*-glycosylglycines **10a**,**b**, **11a**–**c**, **15**. Column chromatography with 3:1 cyclohexane–EtOAc afforded **10a** (104 mg, 67%) as a syrup. $[\alpha]_D$ 32.1 (*c* 1.0, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.20–7.00 (m, 15 H, 3 Ph), 5.96 (d, 1 H, $J_{NH,2}$ = 9.0 Hz, NH), 4.85 (dd, 1 H, $J_{2,NH}$ = 9.0 Hz, $J_{2,3}$ = 2.5 Hz, H-2), 4.65 (dd, 1 H, $J_{3,2}$ = 2.5 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 4.42 and 4.12 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.26 and 4.22 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.21 (s, 2 H, CH_2Ph), 4.14 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 4.0 Hz, H-4), 4.12 (br s, 1 H, H-6), 3.82 (dd, 1 H, $J_{5,4}$ = 4.0 Hz, $J_{5,6}$ = 1.5 Hz, H-5), 3.64 (dd, 1 H, $J_{7a,6}$ = 6.5 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.54 (dd, 1 H, $J_{7b,6}$ = 5.0 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 3.25 (s, 3 H, CH_3), 1.37 (s, 9 H, *t*-Bu). ^{13}C NMR (C_6D_6): δ = 170.2, 156.0, 138.4, 138.0, 137.9, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.4, 127.3, 83.7, 83.2, 82.5, 80.2, 79.1, 73.0, 71.9, 71.3, 67.4, 55.7, 53.0, 51.6, 28.0. MALDI-TOF MS (591.7): *m/z* = 614.6 [M + Na], 630.3 [M + K]. Anal. Calcd for $C_{34}H_{41}NO_8$: C, 69.02; H, 6.98; N, 2.37. Found: C, 69.04; H, 6.97; N, 2.37.

(20) Compound **11a**: $[\alpha]_D$ 27.9 (*c* 0.3, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.25–7.00 (m, 15 H, 3 Ph), 5.94 (d, 1 H, $J_{NH,2}$ = 6.5 Hz, NH), 4.92 (dd, 1 H, $J_{2,NH}$ = 6.5 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 4.45 and 4.15 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.35–4.20 (m, 7 H, 2 CH_2Ph, H-3, H-4 and H-6), 3.83 (br s, 1 H, H-5), 3.79 (dd, 1 H, $J_{7a,6}$ = 6.5 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.68 (dd, 1 H, $J_{7b,6}$ = 5.5 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 3.22 (s, 3 H, CH_3), 1.35 (s, 9 H, *t*-Bu).

Compound **10b**: $[\alpha]_D$ 10.9 (*c* 1.0, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.25–7.00 (m, 15 H, 3 Ph), 5.42 (d, 1 H, $J_{NH,2}$ = 8.5 Hz, NH), 4.92 (dd, 1 H, $J_{2,NH}$ = 8.5 Hz, $J_{2,3}$ = 4.5 Hz, H-2), 4.75 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 4.5 Hz, H-3), 4.32 (ddd, 1 H, $J_{6,5}$ = 4.0 Hz, $J_{6,7a}$ = 6.5 Hz, $J_{6,7b}$ = 5.0 Hz, H-6), 4.28 and 4.19 (2 d, 2 H, *J* = 11.5 Hz, CH_2Ph), 4.26 and 4.21 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.21 and 4.12 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.01 (dd, 1 H, $J_{4,3}$ = 4.5 Hz, $J_{4,5}$ = 2.0 Hz, H-4), 3.87 (dd, 1 H, $J_{5,4}$ = 2.0 Hz, $J_{5,6}$ = 4.0 Hz, H-5), 3.71 (dd, 1 H, $J_{7a,6}$ = 6.5 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.58 (dd, 1 H, $J_{7b,6}$ = 5.0 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b), 3.20 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*-Bu).

Compound **11b**: $[\alpha]_D$ 2.3 (*c* 1.0, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.22–7.00 (m, 15 H, 3 Ph), 5.77 (d, 1 H, $J_{NH,2}$ = 10.0 Hz, NH), 5.33 (dd, 1 H, $J_{2,NH}$ = 10.0 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 4.76 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 5.0 Hz, H-3), 4.49 (ddd, 1 H, $J_{6,5}$ = 4.0 Hz, $J_{6,7a}$ = 7.0 Hz, $J_{6,7b}$ = 5.5 Hz, H-6), 4.32 and 4.25 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.20 and 4.15 (2 d, 2 H, *J* = 11.5 Hz, CH_2Ph), 4.09 (s, 2 H, CH_2Ph), 4.00 (dd, 1 H, $J_{4,3}$ = 5.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 3.84 (dd, 1 H, $J_{5,4}$ = 1.5 Hz, $J_{5,6}$ = 4.0 Hz, H-5), 3.81 (dd, 1 H, $J_{7a,6}$ = 7.0 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.68 (dd, 1 H, $J_{7b,6}$ = 5.5 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b), 3.15 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*-Bu).

Compound **11c**: $[\alpha]_D$ –28.5 (*c* 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.40–7.20 (m, 15 H, 3 Ph), 6.07 (d, 1 H, $J_{NH,2}$ = 9.0 Hz, NH), 4.83 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 5.0 Hz, H-3), 4.74 (dd, 1 H, $J_{2,NH}$ = 9.0 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 4.64 and 4.59 (2 d, 2 H, *J* = 10.5 Hz, CH_2Ph), 4.56 and 4.39 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.54 and 4.47 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.28 (br s, 2 H, H-4 and H-6), 4.03 (t, 1 H, $J_{5,4}$ = $J_{5,6}$ = 5.0 Hz, H-5), 3.54 (s, 3 H, CH_3), 3.53 (dd, 1 H, $J_{7a,6}$ = 4.0 Hz, $J_{7a,7b}$ = 10.5 Hz, H-7a), 3.46 (dd, 1 H, $J_{7b,6}$ = 3.0 Hz, $J_{7b,7a}$ = 10.5 Hz, H-7b), 1.40 (s, 9 H, *t*-Bu).

Compound **15**: $[\alpha]_D$ –6.9 (*c* 0.7, $CHCl_3$). ^1H NMR (C_6D_6): δ = 7.20–7.00 (m, 15 H, 3 Ph), 5.79 (d, 1 H, $J_{NH,2}$ = 9.0 Hz, NH), 5.30 (dd, 1 H, $J_{2,NH}$ = 9.0 Hz, $J_{2,3}$ = 6.0 Hz, H-2), 4.47 (dd, 1 H, $J_{3,2}$ = 6.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 4.31 and 4.24 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.30 and 4.29 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.21 (br s, 1 H, H-6), 4.14 (s, 2 H, CH_2Ph), 4.01 (br s, 1 H, H-5), 3.95 (br s, 1 H, H-4), 3.59 (dd, 1 H, $J_{7a,6}$ = 5.0 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.51 (dd, 1 H, $J_{7b,6}$ = 7.5 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 1.39 (s, 9 H, *t*-Bu).

(21) Cyclization of the *N*-Boc amino alcohol **7c** required two cycles of microwave irradiation to get an acceptable yield of the *C*-furanoside **9c**. On the other hand, microwave irradiation of **5c** for prolonged time periods (single or repeated cycles) did not afford the corresponding furanoside **8c**.

(22) (a) Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *J. Org. Chem.* **1989**, *54*, 702. (b) Dondoni, A.; Orduna, J.; Merino, P. *Synthesis* **1992**, 201.

(23) Reduction of **12** by $NaBH_4$ at lower temperatures and by L-Selectride (THF, –78 °C) afforded the undesired alcohol **7b** as major product.