A novel approach to functionalization of allyl aglycon. Effective synthesis of selectively protected 2-aminoethyl lactoside, a common building block for the synthesis of carbohydrate chains of glycolipids

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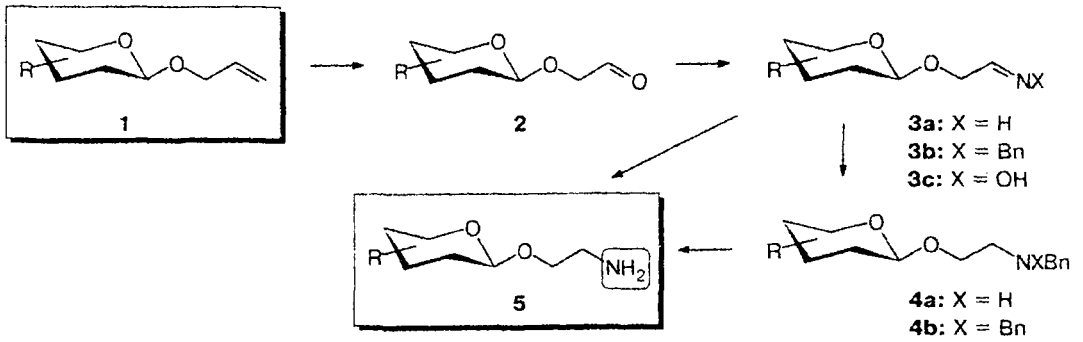
A novel approach to the functionalization of aglycon in allyl glycosides is described. The method comprises ozonolysis of the double bond in the allyl group, leading to the corresponding aldehyde, and subsequent transformation of the latter into the corresponding oxime, which is finally reduced to give the amine. The efficiency of this synthetic sequence (yield ~90%) is exemplified by the transformation of two allyl lactoside derivatives into selectively protected 2-aminoethyl lactosides. The latter are convenient common building blocks for the synthesis of carbohydrate chains of glycolipids that have a lactose unit at the reducing end.

Key words: allyl glycoside; ozonolysis; oximation; reduction; aglycon; pre-spacer; aminoethyl glycosides; glycolipids.

In recent years, oligosaccharides and neoglycoconjugates thereof have been finding ever increasing use in glycobiology and for the preparation of drugs, artificial antigens, diagnosticums, and vaccines.[1] However, three forms of oligosaccharides rather than one form are often required for glycobiological studies. They include (1) reducing oligosaccharides identical to those isolated from natural sources; (2) derivatives with a fixed required (usually "natural") configuration of the anomeric center at the "reducing" end, for example, simple alkyl glycosides; and (3) a "spacered" form with a functional group needed for the preparation of oligosaccharide conjugates with carriers, probes, and other compounds.[2] In recent years, we have been developing an approach based on the use of allyl glycosides as common synthetic precursors of all the above-noted oligosaccharide forms.[3,4] Allyl aglycon has already been used as a "pre-spacer," *i.e.*, an aglycon whose structure allows the introduction of a functional group (primarily, a terminal amino group) at final steps of the synthesis when most of the temporary protective groups have been removed.[2,5–13]

Among the known methods used to introduce an amino group into an allyl aglycon (Scheme 1), reductive amination[6] of aldehyde **2**, formed upon ozonolysis[6,8–12] of allyl glycoside **1**, seems fairly attractive. This process involves the formation and reduction of the corresponding imine (**3a** or **3b**) and gives 2-aminoethyl glycosides **5** [9,11a,13] or their *N*-benzylated derivatives **4a** [11a,13] (see also Ref. 14, describing a similar transformation of *O*-allylcyclodextrins). However, although this process includes few steps, it gives products in moderate yields (50–65%), apparently due to side polyalkylation of the nitrogen atom by the imine present in the reaction

Scheme 1



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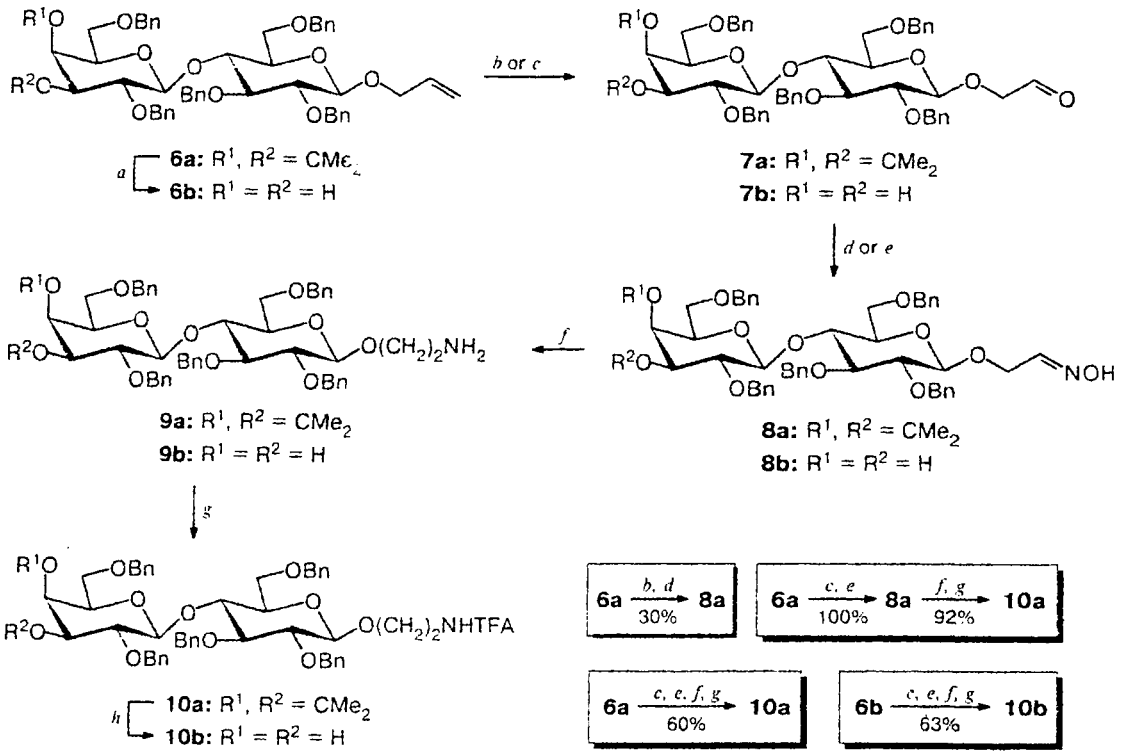
Scheme 2



Reagents and conditions: *a*. AcOH—H_2O (8 : 2), 100 °C; *b*. (1) O_3/CH_2Cl_2—MeOH/−78 °C; (2) Me_2S/−78 °C → 20 °C; *c*. (1) O_3/CH_2Cl_2—MeOH/−78 °C; (2) Ph_3P, −50 °C; *d*. $NH_2OH \cdot HCl$/Py/MeOH/20 °C; *e*. (1) Py; (2) $NH_2OH \cdot HCl$/−50 °C → 15 °C; *f*. $LiAlH_4$/THF/18 → 66 °C; *g*. TFAOEt/Et_3N/MeOH/20 °C; *h*. 90% aq. TFA—CH_2Cl_2 (1 : 9)/20 °C.

mixture. This point of view is supported by the fact that reductive amination of aldehyde **2** by a secondary amine (Bn_2NH) instead of the primary amine gives the corresponding 2-(*N*,*N*-dibenzylamino)ethyl glycoside **4b** [13] in a higher yield (74%); in this case, polyalkylation is impossible.

Meanwhile, it is well known that primary amines can be prepared in high yields by reduction[15] of oximes, readily synthesized from aldehydes. In this work, we investigated the preparative value of this approach for the transformation of allyl glycosides **1** into amines **5** according to the pathway **1** → **2** → **3c** → **5** (Scheme 1). As examples, we chose transformations of allyl glycosides **6a,b** into lactoside **10b**, containing hydroxy groups at C(3′) and C(4′) and a trifluoroacetamide moiety in aglycon, and its precursor **10a** with an isopropylidene protective group. Compounds **10a,b** are convenient synthetic blocks for the preparation of a series of oligosaccharides, in particular, those related to gangliosides and other glycolipids having a lactose unit at the reducing end.

Ozonolysis of allyl glycoside **6a** [16] in a CH_2Cl_2—MeOH (1 : 4) mixture at −78 °C smoothly gave the corresponding methoxyhydroperoxide[17,18]; however, reduction of this product under the typically used conditions (Me_2S, −78→+20 °C)[8a,17] proceeded ambiguously. According to TLC, in addition to the expected aldehyde **7a** (identified from the NMR spectra of the concentrated reaction mixture: δ_H 9.78, δ_C 200.8), the reaction gave, even at −50 °C, a substantial amount of polar side products having lower chromatographic mobilities than **7a**. Apparently, Me_2S reacts with hydroperoxide (or ozonide) rather slowly; therefore, a substantial amount of hydroperoxide remains in the reaction mixture and may oxidize the α-methylene groups of the benzyl protective groups at room temperature to give more polar compounds (selective oxidation of benzyl ethers of alkyl glycosides during ozonolysis is known[19]; meanwhile, ozonolysis of acetylated allyl glycosides occurs without complications[3,8]). Treatment of a methanolic solution of the crude reaction mixture with $NH_2OH \cdot HCl$ in the presence of Py afforded, after chromatographic purification, the corresponding oxime **8a** in 30% yield.

In view of the insufficient reactivity of Me_2S, we used a more reactive reducing agent, Ph_3P. Therefore, the whole sequence of transformations could be conducted at low temperatures, which excluded the possibility of side processes. Thus treatment of the interme-

diate ozonide Ph_3P at −78→−50 °C gave, over a period of 1.5 h, only aldehyde **7a**. The addition of Py and then $NH_2OH \cdot HCl$ to the reaction mixture at −50 °C followed by slow warming to +15 °C yielded only oxime **8a**, which was isolated in a quantitative yield after gel chromatography as a mixture of *syn*- and *anti*-isomers in ~4 : 6 ratio (^1H NMR data).

The structure of oxime was derived from the fact that the NMR spectra of **8a** contained signals of the methine proton and of the carbon atom of the CH=NOH group (δ_H 6.97 and 7.54, δ_C 151.0 and 148.4, *syn*- and *anti*-isomers; *cf.* Ref. 20). The signals of the lactose fragment and protective groups in the ^{13}C NMR spectrum of oxime **8a** have not changed substantially with respect to those in the spectrum of the starting allyl lactoside **6a**, except for the signals for C(1), C(6), and, to a lesser extent, C(6′), which were different for *syn*- and *anti*-isomers.

The oxime **8a** was smoothly reduced on treatment with $LiAlH_4$ in THF to the corresponding 2-aminoethyl glycoside **9a**, which was subsequently transformed (CF_3CO_2Et, MeOH, Et_3N) into the corresponding *N*-trifluoroacetamide derivative **10a** in 92% overall yield. The structure of **10a** followed unambiguously from the presence of signals due to the OCH_2 and NCH_2 groups (δ_C 68.5 and 40.4) in the ^{13}C NMR spectrum of 2-trifluoroacetamidoethyl aglycon (*cf.* Ref. 21), in addition to the signals of the lactose fragment and the protective groups. Deacetonation of **10a** on treatment with aqueous TFA in CH_2Cl_2 resulted in lactoside **10b** in 96% yield.

We also converted compound **6a** into **10a** without purification of the intermediate oxime. In this case, amide **10a** was isolated in 60% yield. Apparently, the lower yield in the case of one-pot synthesis is due to the fact that the resulting oxime **8a** may be contaminated by Ph_3PO, Py · HCl, and $NH_2OH \cdot HCl$. These impurities may hamper quantitative dissolution of **8a** in THF (the crude oxime is a thick syrup only partially soluble in THF), which is necessary for efficient reduction.

Similarly to the synthesis of **10a** from **6a**, we converted **6b** [16] into **10b** along the pathway **6b** → **7b** → **8b** → **9b** → **10b**. The yield of amide **10b** with two hydroxy groups was 63%. Thus, the transformation of allyl glycosides into 2-aminoethyl glycosides *via* the corresponding oximes is also applicable to partially protected sugar derivatives. This result is especially significant because an alternative scheme of functionalization of allyl glycosides based on their ozonolysis, reduction to alcohols, subsequent tosylation, introduction of an azide group, and its transformation into an amino group, which is currently one of the most efficient routes (yields 70—90%),[3] is applicable only to completely protected derivatives of the molecule to be transformed.

Our results indicate that ozonolysis of allyl glycosides followed by the formation of oximes, their reduction, and *N*-trifluoroacetylation according to the pathway **1** → [**2**] → **3c** → **5** is an efficient method for the functionalization of aglycon, the product yields being ~90%. In our opinion, the use of other means of reduction of oximes (for instance, catalytic hydrogenation,[15] inapplicable in this case) would allow one to extend this approach to unprotected allyl glycosides and would markedly extend the scope of this method of functionalization of allyl aglycon.

Experimental

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AM-300 and Bruker DRX-500 instruments, the ^1H chemical shifts are given relative to the residual signal of $CHCl_3$ (δ 7.27), and ^{13}C chemical shifts are referred to the signal of $CDCl_3$ (δ 77.0). All the 2D correlation spectroscopy experiments were carried out using standard Bruker software. Negative ion mass spectra (atmospheric pressure chemical ionization, APCI) were recorded on a Finnigan MAT LCQ instrument. Optical rotation was measured on a JASCO DIP-360 digital polarimeter. Thin layer chromatography was performed on plates with Kieselgel 60 silica gel (Merck); visualization was effected by immersing the plates into a 10% (v/v) solution of 85% H_3PO_4 in 96% EtOH followed by heating to ~150 °C. Column chromatography was carried out on Silica Woelm silica gel (32—63 μm, Woelm Pharma). Gel chromatography was performed on a 50×1.2-cm column with Bio-Beads S-X3 poly(styrene—divinylbenzene) gel (200—400 mesh, Bio-Rad) using toluene at a flow rate of 0.5 mL min^{-1} as the eluent. Ozonolysis was carried out by bubbling an ozone—oxygen mixture (3 mL min^{-1}, 0.36 mmol of ozone min^{-1}). The reagents used were $NH_2OH \cdot HCl$ and $LiAlH_4$ ("Chemically pure grade," Reakhim), CF_3CO_2Et and Ph_3P (Fluka), and Me_2S and TFA (Merck). Acetic acid was distilled from $KMnO_4$ and then from P_2O_5. Pyridine was repeatedly distilled from KOH until the bottom residue was no longer yellow colored. Triethylamine (Merck) was distilled from CaH_2. Tetrahydrofuran was refluxed under argon over Na and benzophenone until a persistent dark-blue color appeared and distilled immediately prior to use. Dichloromethane was distilled twice from P_2O_5 in an argon atmosphere and stored in the dark under argon over 4 Å molecular sieves. Methanol was dried by a standard procedure[22] and stored over 3 Å molecular sieves. The other solvents were distilled prior to use.

Allyl 2,2′,3,6,6′-penta-*O*-benzyl-3′,4′-*O*-isopropylidene-β-D-lactoside (6a). Allyl lactoside **6a** was prepared in an overall yield of 38% by a known procedure[16] from allyl β-D-lactoside[23] as a colorless thick syrup with $[\alpha]_D^{27}$ +15.4° (*c* 5, CH_2Cl_2) and R_f 0.52 (AcOEt—petroleum ether, 3 : 7). Found (%): C, 73.19; H, 6.90. $C_{53}H_{60}O_{11}$. Calculated (%): C, 72.91; H, 6.93. ^1H NMR (^1H—^1H COSY, ^{13}C—^1H COSY), δ: 1.51 and 1.57 (both s, each 3 H, CMe_2); 3.55 (dd, 1 H, H(2′), $J_{1',2'}$ = 7.6 Hz, $J_{2',3'}$ = 7.6 Hz); 3.58 (m, 1 H, H(5)); 3.61 (dd, 1 H, H(2), $J_{1,2}$ = 8.6 Hz, $J_{2,3}$ = 8.6 Hz); 3.74 (m, 1 H, $H_a(6')$); 3.77 (dd, 1 H, H(3), $J_{3,4}$ = 9.1 Hz); 3.85 (m, 1 H, H(5′)); 3.86 (m, 1 H, $H_b(6')$); 3.91 (d, 1 H, $H_a(6)$, $J_{6a,6b}$ = 10.7 Hz); 4.00 (dd, 1 H, $H_b(6)$, $J_{5,6b}$ = 3.9 Hz); 4.18 (dd, 1 H, H(4), $J_{4,5}$ = 10.2 Hz); 4.20 (dd, 1 H, H(3′)); 4.25 (dd, 1 H, H(4′), $J_{3',4'}$ = 10.2 Hz); 4.29 (dd, 1 H, $OC\underline{H}_aH_b$, J = 5.3 Hz, J_{gem} = 13.2 Hz); 4.48 (d, 1 H, $C\underline{H}_aH_bPh^1$, J = 12.1 Hz); 4.55 (m, 1 H, $OCH_a\underline{H}_b$); 4.58 (m, 1 H, $C\underline{H}_aH_bPh^2$); 4.60 (m, 1 H, H(1′)); 4.61 (m, 1 H, H(1)); 4.68 (d, 1 H, $CH_a\underline{H}_bPh^1$, J = 12.1 Hz); 4.75 (m, 1 H, $CH_a\underline{H}_bPh^2$); 4.85 (d, 1 H, $C\underline{H}_aH_bPh^3$, J = 11.9 Hz); 4.90 (d, 1 H, $C\underline{H}_aH_bPh^4$, J = 11.0 Hz); 4.93 (d, 1 H, $C\underline{H}_aH_bPh^5$, J = 10.6 Hz); 4.97 (d, 1 H, $CH_a\underline{H}_bPh^3$, J = 11.9 Hz); 5.08 (d, 1 H, $CH_a\underline{H}_bPh^4$, J = 11.0 Hz); 5.12 (d, 1 H,

$CH_aH_bPh^5$, J = 10.6 Hz); 5.35 (d, 1 H, CH=CH_aH_b, J = 10.4 Hz); 5.50 (d, 1 H, CH=CH_aH_b, J = 17.2 Hz); 6.12 (m, 1 H, CH=CH_2); 7.35–7.60 (m, 25 H, Ph). ^{13}C NMR (^{13}C–^1H COSY, DEPT 135), δ: 26.3, 27.8 (CMe_2); 68.1 (C(6)); 68.8 (C(6′)); 70.0 (OCH_2); 71.9 (C(5′)); 73.00, 73.03, 73.2 (3 CH_2Ph); 73.5 (C(4′)); 74.8 (CH_2Ph); 75.0 (C(5)); 75.2 (CH_2Ph); 76.1 (C(4)); 77.2 (C(3′)); 80.4 (C(2′)); 81.7 (C(2)); 82.8 (C(3)); 102.4, 103.5 (C(1), C(1′)); 109.5 (CMe_2); 116.9 (CH=CH_2); 127.1, 127.2, 127.3, 127.4, 127.5, 127.7, 127.8, 127.9, 127.99, 128.06, 128.10, 128.14, 129.9 (arom. C); 134.0 (CH=CH_2); 138.1, 138.2, 138.4, 138.5, 138.9 (all quat. arom. C).

Allyl 2,2′,3,6,6′-penta-*O*-benzyl-β-D-lactoside (6b). Allyl lactoside **6b** was prepared in 86% yield from **6a** by a known procedure[16] as a colorless thick syrup with $[\alpha]_D^{20}$ +7.6° (*c* 2, $CHCl_3$), +15.6° (*c* 1.15, CH_2Cl_2) (*cf.* Ref. 16) and R_f 0.17 (AcOEt–petroleum ether, 4 : 6). ^1H NMR (^1H–^1H COSY, ^1H–^{13}C COSY), δ: 2.78 (br.s, 2 H, OH); 3.52 (dd, 1 H, H(5′)); 3.56 (br.dd, 1 H, H(5), $J_{5,6a}$ = 1.8 Hz); 3.61 (m, 2 H, H(2′), H(3′)); 3.64 (dd, 1 H, H(2), $J_{1,2}$ = 8.6 Hz); 3.68 (dd, 1 H, $H_a(6')$, $J_{5,6'a}$ = 5.1 Hz, $J_{6'a,6'b}$ = 9.9 Hz); 3.77 (dd, 1 H, H(3), $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz); 3.80 (dd, 1 H, $H_b(6')$, $J_{5',6'b}$ = 6.6 Hz); 3.93 (br.d, 1 H, $H_a(6)$, $J_{6a,6b}$ = 10.1 Hz); 3.99 (dd, 1 H, $H_b(6)$, $J_{5,6b}$ = 4.2 Hz, $J_{6a,6b}$ = 10.9 Hz); 4.09 (br.s, 1 H, H(4′)); 4.19 (dd, 1 H, H(4), $J_{4,5}$ = 9.3 Hz); 4.31 (dd, 1 H, OCH_aH_b, J = 5.9 Hz, J_{gem} = 13.0 Hz); 4.56 (d, 1 H, $CH_aH_bPh^1$, J = 12.0 Hz); 4.62 (m, 6 H, OCH_aH_b, H(1′), H(1), $CH_aH_bPh^1$, $CH_aH_bPh^2$); 4.77 (d, 1 H, $CH_aH_bPh^2$, J = 12.1 Hz); 4.86 (d, 1 H, $CH_aH_bPh^3$, J = 11.6 Hz); 4.90 (d, 1 H, $CH_aH_bPh^4$, J = 10.9 Hz); 4.96 (d, 1 H, $CH_aH_bPh^5$, J = 11.0 Hz); 4.98 (d, 1 H, $CH_aH_bPh^3$); 5.09 (d, 1 H, $CH_aH_bPh^4$); 5.17 (d, 1 H, $CH_aH_bPh^5$); 5.38 (d, 1 H, CH=CH_aH_b, J = 10.4 Hz); 5.51 (d, 1 H, CH=CH_aH_b, J = 17.2 Hz); 6.14 (m, 1 H, CH=CH_2); 7.36–7.58 (m, 25 H, Ph) (for partial ^1H NMR spectrum, see Ref. 16). ^{13}C NMR (^1H–^{13}C COSY, DEPT 135), δ: 68.3 (C(6)); 68.7 (C(6′)); 68.8 (C(4′)); 70.1 (OCH_2); 72.9 (C(5′)); 73.1, 73.4 (2 CH_2Ph); 73.5 (C(3′)); 74.8, 74.9 (2 CH_2Ph); 75.1 (2 C) (C(5), CH_2Ph); 76.5 (C(4)); 80.0 (C(2′)); 81.7 (C(2)); 82.7 (C(3)); 102.5, 102.6 (C(1), C(1′)); 117.1 (CH=CH_2); 127.2, 127.5, 127.6, 127.7, 127.8, 127.9, 127.97, 128.02, 128.2, 128.3, 128.4 (arom. C); 134.1 (CH=CH_2); 138.0, 138.2, 138.4, 138.6, 139.1 (all quat. arom. C).

2-Oximinoethyl 2,2′,3,6,6′-penta-*O*-benzyl-3′,4′-*O*-isopropylidene-β-D-lactoside (8a). ***A.*** At −78 °C, ozone was bubbled for 5 min (persistent blue color of the solution) through a solution of allyl glycoside **6a** (32.0 mg, 37 mmol) in a mixture of CH_2Cl_2 (10 mL) and MeOH (10 mL). The mixture was purged with oxygen (5 min) and argon (1.5 h); TLC analysis showed the formation of a new spot with R_f 0.18 (AcOEt–petroleum ether, 3 : 7). Solid Ph_3P (50 mg, 0.19 mmol) was added at −78 °C to the colorless solution; the mixture was warmed to −50 °C and stirred for 1.5 h at this temperature. Pyridine (0.104 mL, 1.27 mmol) and $NH_2OH \cdot HCl$ (17 mg, 0.26 mmol) were added successively. The reaction mixture was slowly heated to 15 °C (over a period of 18 h) and concentrated, toluene (3×5 mL) was added, and the mixture was concentrated again (×3). Hot toluene (4×5 mL) was added, the mixture was filtered, and the combined filtrate was concentrated. Gel chromatography of the residue gave oxime **8a** (32.8 mg, 100%) as a colorless thick syrup, which was a mixture of *syn*- and *anti*-isomers in a ratio of ~4 : 6 (^1H NMR data). R_f 0.25 (AcOEt–petroleum ether, 3 : 7). Found (%): C, 70.05; H, 6.62; N, 1.53. $C_{52}H_{59}NO_{12}$. Calculated (%): C, 70.17; H, 6.68; N, 1.57. ^1H NMR (only identified signals are presented, ^1H–^1H COSY), δ: 4.28 (dd, 0.6 H, OCH_aH_bCH=NOH, *anti*-isomer, J = 6.0 Hz, J = 13.0 Hz), 4.42 (m, 0.6 H, OCH_aH_bCH=NOH, *anti*-isomer), 4.56 and 4.70 (both m; each 0.4 H, OCH_2CH=NOH, *syn*-isomer), 6.97 (dd, 0.4 H, CH=NOH, *syn*-isomer, J = 3.6 Hz, J = 3.6 Hz), 7.54 (dd, 0.6 H, CH=NOH, *anti*-isomer, J = 6.0 Hz, J = 6.0 Hz). ^{13}C NMR (the signals were assigned by analogy with the spectrum of **6a**), δ: 26.4, 27.9 (CMe_2); 63.8 (~0.4 C, C(6), *syn*-isomer); 66.2 (~0.6 C, C(6), *anti*-isomer); 68.05, 68.14 (~0.5 C each, C(6′), *syn*- + *anti*-isomers); 69.0 (OCH_2); 72.0 (C(5′)); 73.2 (2 C), 73.4 (3×CH_2Ph); 73.6 (C(4′)); 75.06 (CH_2Ph); 75.14 (C(5)); 75.4 (CH_2Ph); 76.1 (C(4)); 79.4 (C(3′)); 80.6 (C(2′)); 81.7 (C(2)); 82.8 (C(3)); 101.8 (C(1′)); 103.6, 103.7 (~0.5 C each, C(1), *syn*- + *anti*-isomers); 109.8 (CMe_2); 127.3, 127.4, 127.5, 127.56, 127.63, 127.8, 127.9, 128.0, 128.17, 128.24, 128.3, 129.7, 129.9 (arom. C); 138.1, 138.4, 138.5, 138.7, 138.9 (all quat. arom. C); 148.4 (~0.6 C, CH=NOH, *anti*-isomer); 151.0 (~0.4 C, CH=NOH, *syn*-isomer).

B. At −78 °C, ozone was bubbled for 5 min (persistent blue color of the solution) through a solution of allyl glycoside **6a** (332 mg, 0.38 mmol) in a mixture of CH_2Cl_2 (10 mL) and MeOH (40 mL). The mixture was purged with oxygen (5 min) and argon (30 min); TLC analysis showed the formation of a new spot with R_f 0.18 (AcOEt–petroleum ether, 3 : 7). Dimethyl sulfide (3 mL, 0.04 mol) was added at −78 °C to the colorless solution, the mixture was stirred for 20 min at this temperature, allowed to slowly warm up to 20 °C (over 1.5 h), and concentrated, CH_2Cl_2 (3×10 mL) was added, and the mixture was concentrated again (×3) and dried *in vacuo*. After NMR (δ_H 9.78, δ_C 200.8) and TLC analyses (two spots: R_f 0.18 and R_f ~0), solid $NH_2OH \cdot HCl$ (137 mg, 2.13 mmol) was added to the product. Methanol (5 mL) and Py (5 mL, 61.8 mmol) were added under argon. The resulting solution was stirred under argon at 20 °C for 18 h and concentrated, toluene (3×10 mL) was added, and the mixture was concentrated again (×3) and dried *in vacuo*. Chromatography of the residue on silica gel (elution with AcOEt–petroleum ether, 4 : 6) gave oxime **8a** (101.5 mg, 30%) with chromatographic mobility and NMR spectra identical to those of the sample prepared by method ***A***.

2-Trifluoroacetamidoethyl 2,2′,3,6,6′-penta-*O*-benzyl-3′,4′-*O*-isopropylidene-β-D-lactoside (10a). ***A.*** A solution of oxime **8a** (24 mg, 27 μmol) in THF (4 mL) was added under argon to a suspension of $LiAlH_4$ (28 mg, 0.74 mmol) in THF (5 mL). The mixture was stirred at 20 °C for 18 h and refluxed for 2 h. On cooling (4 °C), H_2O (30 μL), 20% NaOH (22 μL), and again H_2O (103 μL) were added. The suspension was stirred at 20 °C for 1.5 h and filtered through a Celite pad. The precipitate was washed with THF (30 mL) and MeOH (10 mL). The filtrate was concentrated and dried *in vacuo*. Anhydrous MeOH (5 mL), Et_3N (100 μL, 0.72 mmol), and CF_3CO_2Et (50 μL, 0.42 mmol) were added to the residue (84 mg). The mixture was stirred at 20 °C for 15 h and concentrated. Chromatography on silica gel (elution with AcOEt–petroleum ether, 15 : 85) gave amide **10a** (24.0 mg, 92%) as a colorless thick syrup with $[\alpha]_D^{27}$ +15.3° (*c* 1, $CHCl_3$) and R_f 0.63 (AcOEt–petroleum ether, 4 : 6). MS *m/z* (*I* (%)): 970.5 (92) $[M - H]^-$, 971.6 (36) $[M + 1 - H]^-$, 880.4 (100) $[M - CH_2Ph]^-$, 881.2 (77) $[M + 1 - CH_2Ph]^-$, 882.0 (41) $[M + 2 - CH_2Ph]^-$. $C_{54}H_{60}F_3NO_{12}$. Calculated: M = 971.41; for the $[M - CH_2Ph]^-$ ion, 880.35; for the $[M + 2 - CH_2Ph]^-$ ion, 882.37. ^1H NMR (^1H–^1H COSY, ^1H–^{13}C COSY), δ: 1.36 and 1.42 (both s, each 3 H, CMe_2); 3.35 (dd, 1 H, H(2′), $J_{1',2'}$ = 8.0 Hz, $J_{2',3'}$ = 6.8 Hz); 3.38 (dd, 1 H, H(2), $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 9.0); 3.43 (m, 1 H, H(5)); 3.46 (m, 2 H, CH_2N); 3.51 (m, 1 H, $H_a(6')$); 3.57 (dd, 1 H, H(3), $J_{3,4}$ = 10.0 Hz); 3.67 (m, 2 H, H(5′), $H_b(6')$); 3.73 (m, 2 H, H(6)); 3.85 (m, 2 H, OCH_2); 3.89 (dd, 1 H, H(4), $J_{4,5}$ = 10.0 Hz); 4.04 (dd, 1 H, H(3′)); 4.12 (dd, 1 H, H(4′), $J_{3',4'}$ = 5.8 Hz, $J_{4',5'}$ = 2.0 Hz);

4.28—4.37 (m, 4 H, H(1), H(1′), $C\underline{H}_aH_bPh^1$, $C\underline{H}_aH_bPh^2$); 4.48 (d, 1 H, $CH_a\underline{H}_bPh^2$, J = 12.3 Hz); 4.51 (d, 1 H, $CH_a\underline{H}_bPh^1$, J = 12.0 Hz); 4.63 (d, 1 H, $C\underline{H}_aH_bPh^3$, J = 11.9 Hz); 4.71—4.83 (m, 4 H, $C\underline{H}_aH_bPh^4$, $C\underline{H}_2Ph^5$, $CH_a\underline{H}_bPh^3$); 4.97 (d, 1 H, $CH_a\underline{H}_bPh^4$, J = 10.8 Hz); 7.20—7.40 (m, 25 H, Ph). ^{13}C NMR (^1H–^{13}C COSY, DEPT 135), δ: 26.4, 27.9 ($C\underline{Me}_2$); 40.4 (CH_2N); 68.3 (C(6)); 68.5 (OCH_3); 68.9 (C(6′)); 72.1 (C(5′)); 73.1, 73.2, 73.3 (3 $\underline{C}H_2Ph$); 73.5 (C(4′)); 74.8 (C(5)); 75.1, 75.4 (2 $\underline{C}H_2Ph$); 76.5 (C(4)); 79.3 (C(3′)); 80.6 (C(2′)); 81.5 (C(2)); 82.8 (C(3)); 101.9 (C(1)); 103.7 (C(1′)); 109.8 ($\underline{C}Me_2$); 127.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.16, 128.21, 128.25, 128.32 (arom. C); 137.7, 138.23, 138.28, 138.4, 138.7 (all quat. arom. C).

B. Ozonolysis of allyl glycoside **6a** (217.2 mg, 0.25 mmol) in a mixture of CH_2Cl_2 (20 mL) and MeOH (20 mL) and the subsequent reactions with Ph_3P (390 mg, 1.47 mmol) and $NH_2OH \cdot HCl$ (136 mg, 2.11 mmol) in the presence of Py (0.85 mL, 10.53 mmol), carried out after concentration of the reaction mixture, were performed as described for the synthesis of **8a** (procedure ***A***). This gave a mixture containing oxime **8a** (TLC data), which was used without chromatographic purification. Treatment of this mixture with $LiAlH_4$ (386 mg, 10.17 mmol) in THF (36 mL) and then with Et_3N (100 μL, 0.72 mmol) and CF_3CO_2Et (50 μL, 0.42 mmol) in anhydrous MeOH (5 mL), as described for the synthesis of **10a** (procedure ***A***), gave, after chromatography on silica gel, amide **10a** (144.6 mg, 60%) with chromatographic mobility and NMR spectra identical to those of the sample prepared by method ***A***.

2-Trifluoroacetamidoethyl 2,2′,3,6,6′-penta-*O*-benzyl-β-D-lactoside (10b). ***A.*** A 90% solution of TFA in water (2.2 mL) was added to a solution of acetonide **10a** (137.1 mg, 0.14 mmol) in CH_2Cl_2 (9.8 mL) and the mixture was kept at 20 °C. After 20 min, the solution was concentrated, toluene (3×5 mL) was added, and the mixture was concentrated again (×3). Chromatography of the residue on silica gel (elution with AcOEt—petroleum ether, 1 : 1) gave diol **10b** (125.9 mg, 96%) as a colorless thick syrup with $[\alpha]_D^{20}$ +16.3° (*c* 0.76, $CHCl_3$) and R_f 0.35 (AcOEt—petroleum ether, 1 : 1), 0.53 (AcOEt—benzene, 1 : 1). Found (%): C, 65.73; H, 6.12; N, 1.51. $C_{51}H_{56}F_3NO_{12}$. Calculated (%): C, 65.73; H, 6.06; N, 1.50; M = 931.38. MS, *m/z* (*I* (%)): 962.3 (100) $[M + MeOH - H]^-$, 963.1 (56) $[M + 1 + MeOH - H]^-$. Calculated for the $[M + MeOH - H]^-$ ion, $C_{52}H_{59}F_3NO_{13}$, 962.39. ^1H NMR (^1H–^1H COSY, the signals were assigned by analogy with those for **6b** and **10a**), δ: 2.45 (br.s, 2 H, OH); 3.37 (m, 1 H, H(5′)); 3.42 (m, 2 H, H(2′), H(3′)); 3.45 (m, 2 H, H(2), H(5)); 3.53 (m, 3 H, H_a(6′), CH_2N); 3.62 (m, 1 H, H(3)); 3.63 (m, 1 H, H_b(6′)); 3.77 (m, 2 H, H(6)); 3.87 (m, 2 H, OCH_3); 3.97 (m, 2 H, H(4), H(4′)); 4.35—4.60 (m, 4 H, $C\underline{H}_2Ph^1$), $C\underline{H}_2Ph^2$); 4.39 (d, 1 H, H(1′), $J_{1',2'}$ = 5.7 Hz); 4.44 (d, 1 H, H(1), $J_{1,2}$ = 7.3 Hz, H(1)); 4.65—4.85 (m, 5 H, $C\underline{H}_2Ph^3$), $C\underline{H}_2Ph^4$, $C\underline{H}_aH_bPh^5$); 5.02 (d, 1 H, $CH_a\underline{H}_bPh^5$, J = 11.0 Hz); 7.20—7.40 (m, 25 H, Ph). ^{13}C NMR (the signals were assigned by analogy with those for **6b** and **10a**), δ: 40.4 (CH_2N); 68.3 (C(6)); 68.6 (C(6′)); 68.7 (OCH_3); 68.8 (C(4′)); 72.9 (C(5′)); 73.2 ($\underline{C}H_2Ph$); 73.5 (2 C) ($\underline{C}H_2Ph$, C(3′)); 74.8, 74.9, 75.1, 75.2 (3×$\underline{C}H_2Ph$, C(5)); 76.7 (C(4)); 80.0 (C(2′)); 81.5 (C(2)); 82.7 (C(3)); 102.7 (C(1)); 103.6 (C(1′)); 127.3, 127.6, 127.7, 127.9, 128.1, 128.4, 128.5 (arom. C); 137.6, 137.8, 138.2 (2 C), 138.8 (all quat. arom. C).

B. Similarly to the synthesis of **10a** (procedure ***B***), allyl lactoside **6b** (44.3 mg, 53.2 μmol) was converted *via* ozonolysis, oximation, reduction, and *N*-trifluoroacetylation into amide **10b** (31.2 mg, 63%) with chromatographic mobility and NMR spectra identical to those of the sample prepared by method ***A***.

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