First Preparation of Spacer-Linked Cyclic Neooligoaminodeoxysaccharides

Guang-wu Chen[b] and Andreas Kirschning*[a]

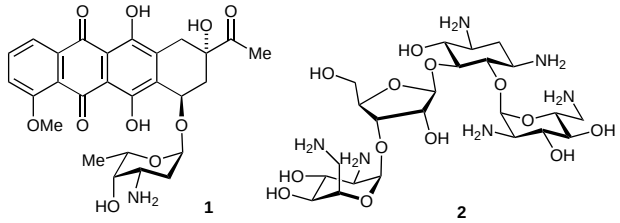
Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 70th birthday

Abstract: The preparation of novel cyclic 1,4-butanediol-linked oligoaminodeoxysugars **3**–**5** and **7** is described which are potential binders to polynucleotides. Neooligosaccharides **3**–**5** are assembled by two consecutive metathesis protocols. In the first phase metathesis-mediated dimerization of an aminodeoxymonosaccharide which was either allylated at the anomeric center or at C4 led to *E*/*Z* mixtures of C_2-symmetric homodimers which were transformed into the corresponding 1,4-butanediol linked disaccharides by catalytic hydrogenation of the central olefinic double bond. Double O-allylation of the head-to-head dimer set the stage for macrocyclization by means of ring-closing metathesis. This ring-closing process was highly dependent of the configuration in the carbohydrate moieties. *arabino*-Configured homodimer **15** directly yielded the macrocycle **32** which contains two sugar units while under the same metathesis conditions the corresponding *ribo*-configured starting homodimer **19** afforded cyclic neotetra- and neohexasaccharides **34** and **35** after a preceding dimerization and trimerization step, respectively. In addition, homodimer **23** was coupled with silylglycoside **14a** under Lewis-acid promoted glycosidation conditions to furnish the doubly glycosylated homodimer **31**. Ring-closing metathesis afforded the macrocyclic neoaminodeoxyoligosaccharide **36** with alternating 1,4-butanediol linkage and glycosidic bond. The primary cyclization products were finally transformed into the respective cyclic neoaminodeoxyoligosaccharides **3**–**5** and **7** by catalytic hydrogenation and standard deprotection conditions.

Keywords: antibiotics · carbohydrates · glycosidation · macrocycles · metathesis

Introduction

Oligocationic compounds such as protonable polyamines can play a key role in biological processes. Their pharmacological activity is associated with their ability to specifically bind to polynucleotides, thus giving rise to the possibility of inhibiting DNA duplication[1] or RNA catalysis, or the forcing of RNA into an alternate conformation.[2, 3] Indeed, nature has utilized aminodeoxy sugars present in glycoconjugates such as the anthracycline antibiotic daunomycin (**1**) as well as amino glycoside antibiotics such as neomycin B (**2**) to target polynucleotides. In this context, the interactions between aminoglycosides and various RNA targets have been investigated (group I intron and *Rev*-response element,[4] the TAR-RNA,[5] ribosomal "A-site",[6] hammerhead ribozyme[7] and other polynucleotide targets[8]). The results of most of these studies suggest that RNA regions containing either asymmetric internal loops or hairpin loop-stem junctions are preferential binding sites for aminoglycosides. The major drawback of aminoglycosides in medicinal applications, however, is their significant toxicity. Nevertheless, their basic scaffold together with a variety of different techniques for joining monomeric subunits make them ideal for the synthesis of new selective and potentially less toxic structures that can be used for studying RNA binding.



1 **2**

This scenario was the starting point of our synthetic efforts in this field with the intention to design and construct novel linear and cyclic "artificial" aminoglycosides. Thus, we recently initiated a project on the preparation of new 1,4-butanediol-linked oligomeric aminodeoxysugars.[9] These novel structures consist of aminodeoxysugar-based pyran rings which are linked to each other by a flexible element

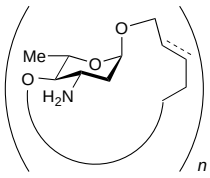
[a] Prof. Dr. A. Kirschning
Institut für Organische Chemie, Universität Hannover
Schneiderberg 1B, 30167 Hannover (Germany)
Fax: (+49) 511-762 4614
E-mail: andreas.kirschning@oci.uni-hannover.de

[b] Dr. G.-w. Chen
Institut für Organische Chemie
Technische Universität Clausthal, Leibnizstrasse 6
38678 Clausthal-Zellerfeld (Germany)

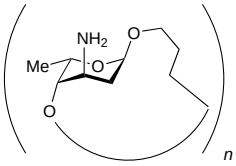
  0947-6539/02/0812-2717 $ 20.00+.50/0

hence yielding linear spacer-linked neooligosaccharides.[9, 10] Their oligomeric character in association with the larger number of amino groups which are essential for efficient binding should lead to cooperative effects[11] and hence tighter binding.

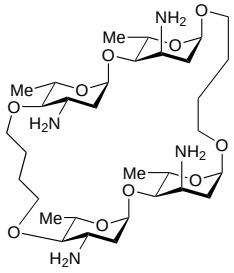
As an extention to these linear neooligoaminodeoxysaccharides[9] we now report the first preparation of novel cyclic 1,4-butanediol-linked neooligoaminodeoxysaccharides **3**–**5** as well as **7** and disclose a synthetic route that leads to macrocyclic hexasaccharide **6**. The 1,4-butane diol linkage between two adjacent aminodeoxysugar moieties in the macrocycle is efficiently constructed by metathesis-based alkene dimerization[12] of appropriately allylated glycosides using the Grubbs precatalyst **8** (see Scheme 1).



3: *n* = 2, unsat. linker
4: *n* = 2, sat. linker



5: *n* = 4
6: *n* = 6



7

Results and Discussion

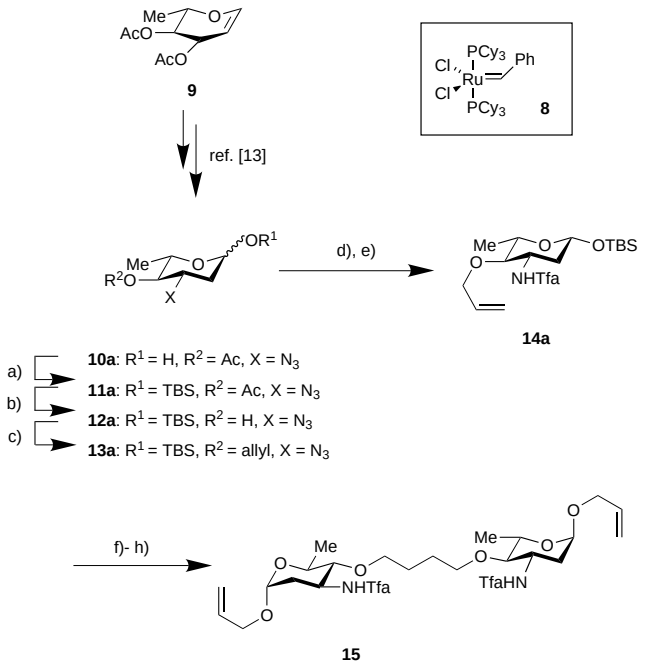
In the first phase of the project we had to develop synthetic access to various homodimeric spacer-linked aminodeoxysaccharides containing two terminal double bonds. These functionalities served as reactive groups for the ring closing metathesis macrocyclization.

Glycal **9** served as the starting carbohydrate-based building block for the synthesis of all macrocyclic oligoaminodeoxysaccharides described in this report. Thus, *arabino*-configured pyranose **10a** was isolated as the major product out of four isomeric products **10a**–**10d** by employing the protocol developed by Monneret and co-workers (Scheme 1).[13] The synthesis towards homodimeric 1,4-butanediol-linked L-acosamine derivative **15** was further elaborated by O-silylation[14, 15] of the anomeric centers in **10a**–**10d** to yield a mixture of silylglycosides *β-arabino* **11a**, *β-ribo* **11b**, *α-arabino* **11c**, and *α-ribo* **11d** from which only the *α-ribo*-configured isomer **11d** was separated by chromatography (3.4% yield from L-rhamnal **9**). The remaining mixture of silyl glycosides **11a**–**11c** was subjected to hydrolysis thereby removing the 4-*O*-acyl groups furnishing silyl glycosides **12a**–**12c** of which only the major isomer **12a** is depicted in Scheme 1. These isomers were also conveniently separated by column chromatography on a larger scale. The *arabino*-configured alcohol **12a** was obtained in 61% yield (from L-rhamnal **9**). In addition the the remaining *β-ribo* **12b** (28%) and *α-arabino* **12c** (1.0%) isomers were collected in pure form.[16] O-Allylation was achieved by sodium hydride-mediated deprotonation and addition of allyl bromide. Subsequently, the azido group in allyl ether **13a** was reduced to the corresponding amino group[17] which then was directly protected as the corresponding trifluoroacetamide **14a**. Now the stage was set for the first metathesis dimerization using precatalyst **8**. Under the conventional conditions tail-to-tail dimerization proceeded in satisfactory yield (70%) leading to an *E*/*Z* mixture (6:1) of stereoisomers. The classical Grubbs catalyst **8** turned out to be insensitive towards the various polar functionalities such as the trifluoroacetamido group and the anomeric silyl ether present in glycoside **14a**. As expected, the ^{1}H NMR and ^{13}C NMR spectra of C_2-symmetric homodimeric reaction product **17** showed only half the set of signals for all protons as well as carbon atoms.[18] Further structural support was gained from proton integration and mass spectrometry. Careful chromatographic purification revealed two additional by-products. Thus, monosaccharide **16** (11%; *E*/*Z* ratio about 1:1) only differs from starting allyl glycoside **14a** in that it contained a shifted alkenic double bond and hence an enol ether functionality. It is obvious that the catalyst is not only able to promote dimerization but also shows some activity in terms of double bond migration. The 1,2-disubstituted enol ether double bond is not reactive enough to get involved in a metathesis process so we were unable to isolate a dimer originated from glycoside **16**. This view is further supported by the isolation of minor amounts of unsymmetric dimer **18** (8%). Again, the formation of the enol ether double bond very likely originated from a double bond migration in homodimer **17** and was catalyzed by the Grubbs catalyst **8**. The formation of these unexpected enol ethers preferentially occurs at elevated reaction temperatures. This property of catalyst **8** is closely related to the prototropic rearrangement of allyl ethers to the corresponding 1-propenyl analogues, which was described for various transition metal complexes such as the Tebbe reagent,[19] rhodium catalysts[20] and $PdCl_2$, $RuCl_3$ and $IrCl_3$.[21]

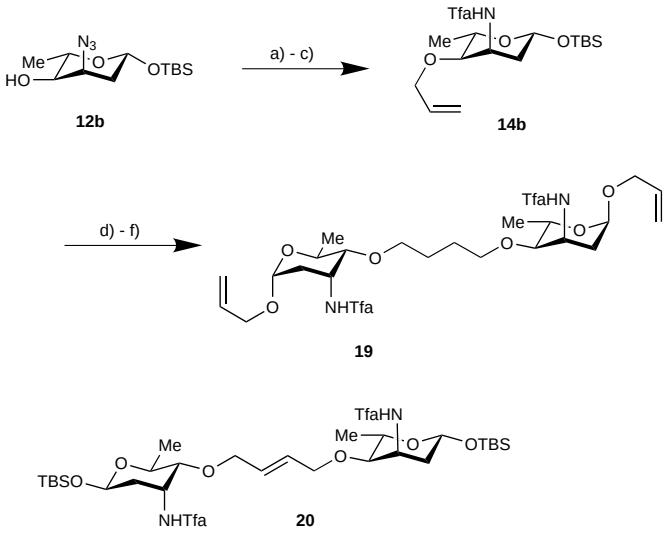
The synthesis was terminated by catalytic hydrogenation of the alkenic double bond which can be performed with both dimers **17** and **18**. This was followed by a silyl triflate-mediated double glycosidation of the two anomeric centers using an excess of allyl alcohol as glycosyl acceptor. Both glycosidation steps proceeded in a highly *α*-selective fashion (even traces of the *α*,*β*- and *β*,*β* diastereomers could not be isolated). The experiment yielded the bisallyl acosamide **15** in a remarkably high yield (89%).

In analogy to Scheme 1, the corresponding homodimeric *ribo*-configured analogue **19** was prepared (Scheme 2). In this case, silyl glycoside **12b** was the starting material, which was the second most abundant isomer isolated from the reaction mixture of the three-step sequence (see Scheme 1). Silver oxide-promoted allylation of the hydroxy group at C-4 afforded silyl glycoside *β-ribo* **13b** which was reduced to the amine and finally protected as trifluoroacetamide **14b**. Dimerization to homodimer **20** proceeded in 62% yield (*E*/*Z* ratio > 20:1). The sequence was terminated by catalytic hydrogenation of the double bond followed by Lewis

  0947-6539/02/0812-2718 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

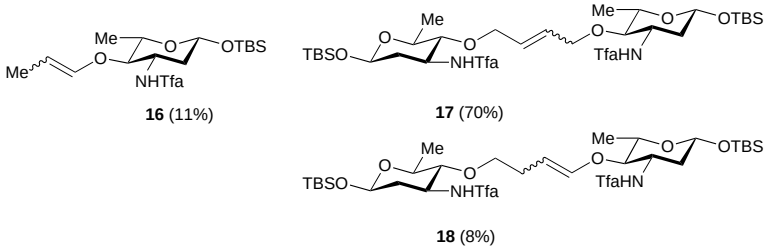


Scheme 1. Preparation of 1,4-butanediol linked C_2-symmetric *arabino*-configured allyl glycoside **15**. a) TBSCl, imidazole, CH_2Cl_2, 0 °C, 6 h; b) MeOH, MeONa, RT, 5 h (61 % from **9**)[16]; c) allyl bromide, NaH, THF (99 %); d) $LiAlH_4$, Et_2O; e) $(Tfa)_2O$, Et_3N, CH_2Cl_2, 0 °C (56 % for two steps); f) **8** (9.8 mol %), C_6H_6, 45 °C, 20 h (78 % for **17** and **18**); g) H_2, PtO_2, ethyl acetate, RT, 14 h (95 %); h) allyl alcohol (excess), TMSOTf (0.6 equiv), MS, CH_2Cl_2, −60 to −30 °C, 16 h (89 %).

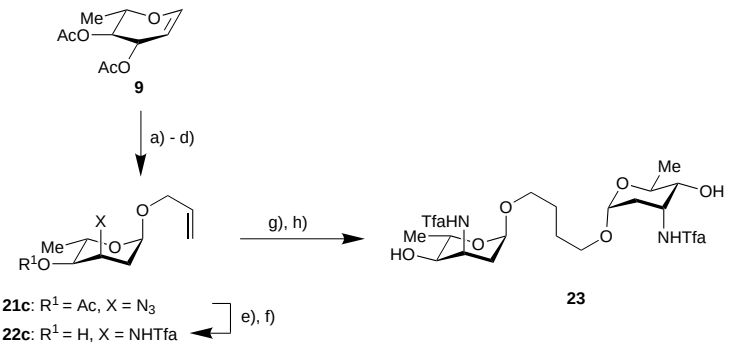


Scheme 2. Preparation of 1,4-butanediol linked C_2-symmetric *ribo*-configured allyl glycoside **19**. a) allyl iodide, Ag_2O, CH_3CN, 50 °C, 20 h (24 % of **13b**); b) $LiAlH_4$, THF, RT, 2 h; c) $(Tfa)_2O$, Et_3N, CH_2Cl_2, 0 °C (78 % for two steps); d) **8** (13.1 mol %), C_6H_6, 40 – 50 °C, 20 h (62 % of **20**); e) H_2, PtO_2, ethyl acetate, RT, 14 h (87 %); f) allyl alcohol, TMSOTf (0.6 equiv), MS, CH_2Cl_2, −60 to −40 °C, 15 h (88 %).

acid-promoteddouble glycosidation with allyl alcohol to furnish homodimeric spacer-linked bis-ristosamide **19**.[22] The yield for the key dimerization step was lower in comparison to the *arabino*-configured silyl glycoside **14a**. This fact has to be ascribed to the axially oriented trifluoroacetamido substituent an observation that we also noted for related systems (see above).

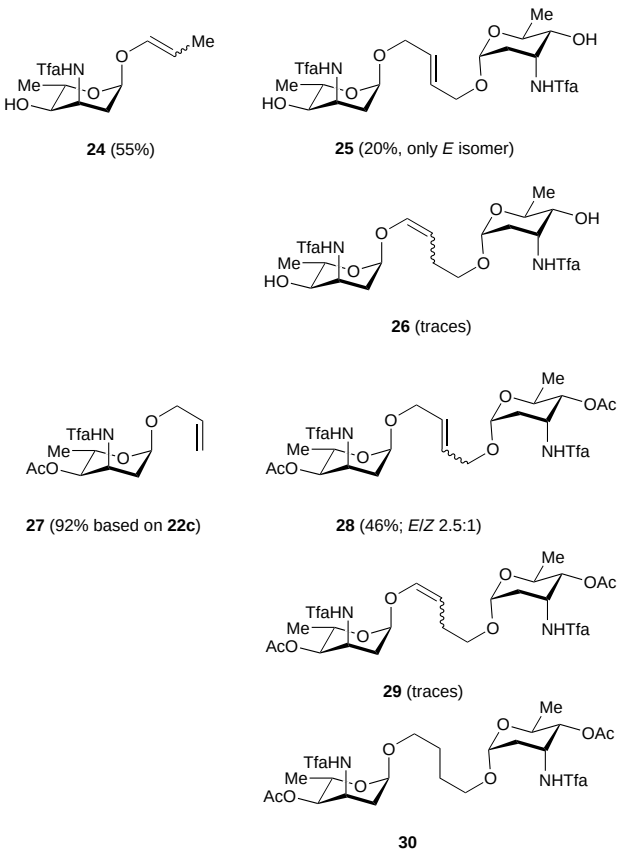


In a third synthesis towards the spacer-linked ristosamine-based dimer **23**, L-rhamnal **9** again served as the starting point (Scheme 3). Azidation was achieved as described before (see Scheme 1 and ref. [13]). The four isomeric 3-azido pyranoses **10a–d** were transformed into the corresponding allyl glycosides either by direct acid-catalyzed allylation[23] (40 % from L-rhamnal **9**) using ion-exchange resins or alternatively by 1-*O*-acylation under standard conditions followed by allylation using montmorillonite K 10 (65 % from L-rhamnal **9**).[24] At this point, three isomeric allyl glycosides were separated by column chromatography (*α-arabino* **21a**: 49 %; *β-arabino* **21b**: 9 %, and *α-ribo* **21c**: 7 %) (in Scheme 3 only **21c** is depicted). The second most abundant isomer, the *α-ribo*-configured ristosaminide **21c**, was used subsequently. This was possible because the reaction sequence could easily be scaled up to 20 g without reduced efficacy. Then, the azido group was reduced first and the intermediate amino group was immediately blocked as trifluoroacetamide. Saponification of the trifluoroacetyl ester was achieved in methanol[25] to yield allyl glycoside **22c**. The moderate yields of this three-step sequence was due to difficulties after workup of the reduction step. Complete removal of all traces of aluminium salts was essential for best results. Notably the modification of the nitrogen functionality was necessary at this point because the azido functionality was not tolerated under the metathesis olefination condition that was going to follow. In the presence of precatalyst **8**, dimerization of allyl glycoside **22c** proceeded with low yield for homodimer **25** but with high stereoselectivity (20 %; only *E* isomer). Again, rearranged starting pyranoside **24** (55 %) and rearranged dimeric enol ether **26** (traces) were formed as additional products. Due to the inefficiency of this process we investigated metathesis olefination of the allyl glycoside **27** which can simply be obtained from alcohol **22c** in 92 % yield after acylation under standard conditions (Ac_2O, Et_3N, cat. 4-DMAP, CH_2Cl_2, RT, 1 h). Indeed, under the usual metathesis conditions [**8** (9.1 mol %), benzene, 50 °C, 10 h] dimerization proceeded more smoothly compared with allyl glycoside **22c** yielding homodimer **28** (46 %, *E*/*Z* ratio 2.5:1) along with traces of enol ether **29**. The alkenic double bonds in dimer **25** as well as in enol ether **26** were hydrogenated to afford target homodimer **23**. Likewise, the 4-*O*-acylated



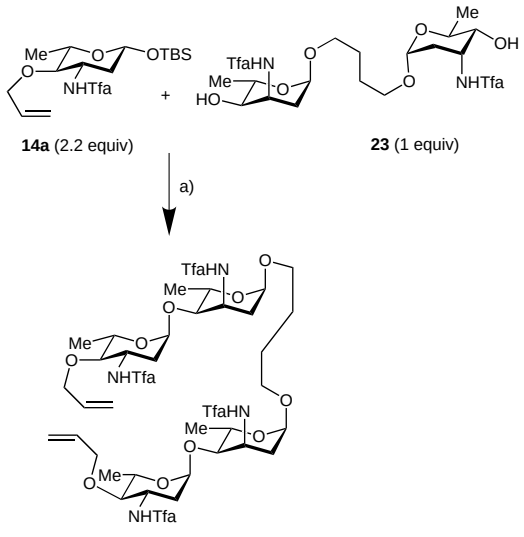
Scheme 3. Preparation of head-to-head linked C_2-symmetric glycoside **23**. a) H_2O, 80 °C; b) NaN_3, HOAc, H_2O, 80 °C then c) either allyl alcohol, 90 °C, 1 h, Dowex-50 (H^+ form), (40 %) or Ac_2O, py, CH_2Cl_2, 10 h; d) allyl alcohol, C_6H_6, Δ, K 10 montmorillonite, 12 h (53 %); e) $LiAlH_4$, THF, 0 °C, 2 h; f) $(CF_3CO)_2O$, Et_3N, CH_2Cl_2, 1 h, then allyl acohol, RT, 2 h (29 %); g) **8** (8.3 mol %), C_6H_6, 50 °C, 10 h [**25** (20 %) only *E* isomer, **26** (traces), **24** (55 %)]; h) PtO_2, H_2, ethyl acetate, RT, 16 h (73 %).

analogues **28** and **29** can also be transformed into 1,4-butanediol-linked bis-L-ristosaminide **23** by means of catalytic hydrogenation (PtO_2, H_2, ethyl acetate, rt, 16 h; 89 %) and mild ester hydrolysis [0.1M NaOH/THF (3:1), RT, 0.5 h; 94 %]. The dimerization of the *arabino*-configured



analogue of allylglycoside **27** with an all equatorial substitution pattern proceeds in 90 % yield using only 5.5 mol % of the catalyst **8**[25] clearly indicating that the efficacy of the coupling is highly dependent on both the configuration of the substituent at C-3 as well as the number of functional groups with hydrogen bonding properties (4-OH versus 4-OAc). The presence of a polar hydroxy group seems to deactivate the ruthenium benzylidene complex. This observation contrasts some of the work published in this field. For example, the immunosuppressive natural product FK506[26] was successfully homodimerized. Also the ring-closing metathesis of the disaccharide subunit of tricolorin A described by Fürstner and co-workers was achieved in the presence of free alcohol groups.[27] Therefore, we reckoned that it is the combination of the free hydroxy group and trifluoroacetamido group which is able to deactivate the Ru-carbene complex **3** by chelation thus effectively shutting down the catalytic cycle.[28]

In order to enhance structural variations in the macrocyclic neooligosaccharides we planned to incorporate "true" glycosidic bonds into the ring-closing precursor. This structural element is typically present in natural carbohydrate-derived macrocycles, the cyclodextrins. Thus, we envisaged the preparation of a macrocyclic oligoaminodeoxysaccharide containing a disaccharide unit with two different sugar components based on α-L-ristosamine and α-L-acosamine. The linear heterogeneous precursor for this macrocycle was prepared from the head-to-head homodimer **23**. This compound served as glycosyl acceptor in the Lewis acid promoted glycosidation with silyl glycoside **14a** (Scheme 4). Under the common glycosidation conditions developed for silyl glycosides[14, 15] the C_2-symmetric acceptor was glycosylated twice to yield homodimer **31** which we reckoned to be another suitable starting material for the ring-closing metathesis reaction. The process was highly α-selective with respect to both glycosidation reactions.

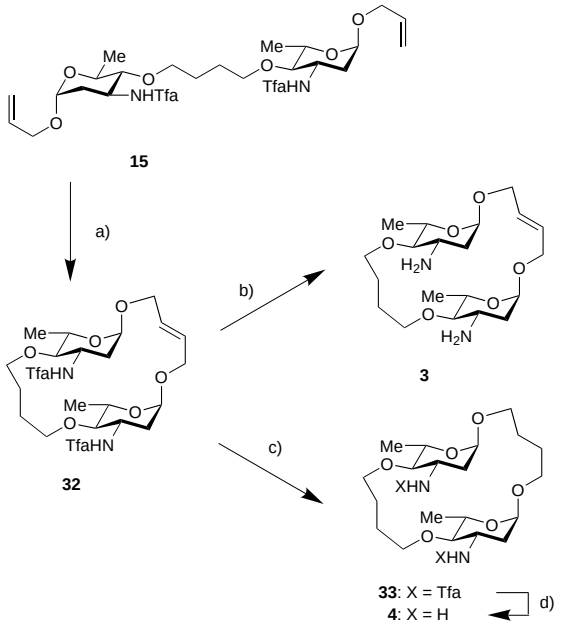


Scheme 4. Preparation of 1,4-butanediol linked C_2-symmetric tetrasaccharide **31**. a) TMSOTf (two portions: 0.72 equiv and 0.36 equiv), MS, CH_2Cl_2, −60 to −40 °C, 20 h (78 %).

  0947-6539/02/0812-2720 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

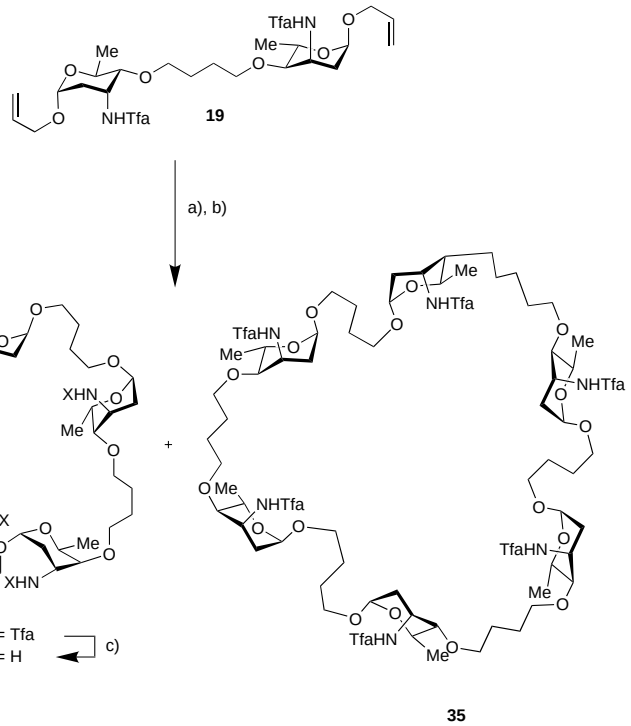
Now, three different types of neooligosaccharides **15**, **19**, and **31** were at hand each containing two terminal alkenes, but differing in configuration and mode of connectivity. Thus, homodimers **15** and **19** are tail-to-tail dimers with the terminal olefinic double bonds located close to the anomeric center. In contrast, linear neotetrasaccharide **31** contains a typical glycosidic bond as part of a disaccharide subunit which is dimerized in the head-to-head mode while the olefinic double bonds are attached via an ether linkage at C-4 of the terminal hexoses.

These three neooligosaccharides were then subjected to metathesis-based macrocyclization conditions. In the first attempt, L-acosamine-based bisallyl glycoside **15** was cyclized to yield a single stereoisomer **32** with remarkable yield (67 %) (Scheme 5). In addition, homodimer **15** was recovered in 20 % yield. Hydrolysis of the amide groups in the macrocycle **32** under basic conditions gave the first unsaturated cyclic spacer-linked aminodeoxydisaccharide **3**. Alternatively, catalytic hydrogenation of the olefinic double bond in macrocycle **32** led to compound **33** which was further transformed to the corresponding saturated cyclic neodisaccharide **4** under the standard hydrolytic conditions (aq. NaOH).



Scheme 5. Macrocyclization of C_2-symmetric *arabino*-configured allyl glycoside **15** by ring closing metathesis. a) **8** (20 mol %), dry C_6H_6, 47 °C, 24 h (67 %); b) aq. NaOH (0.1 M)/THF (3:1), RT, 5 h (94 %); c) PtO_2, H_2, CH_2Cl_2/MeOH (10:1), RT, 16 h (87 %); d) aq. NaOH (0.1 M)/THF (3:1), RT, 5 h (85 %).

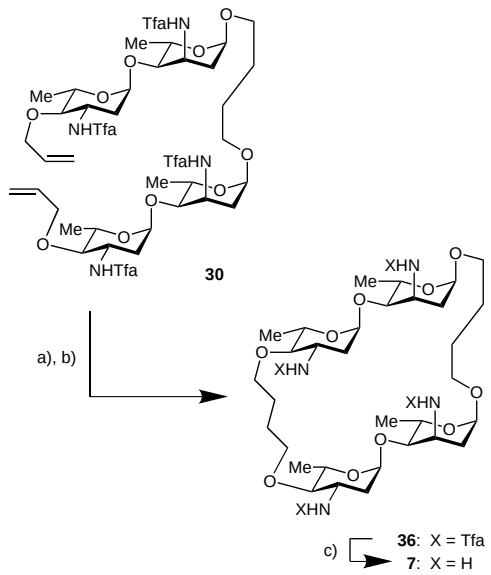
The next macrocyclization revealed that subtle structural alterations in the aminodeoxyhexose moiety, such as the relative configuration of the substituents on the pyran ring and the mode of connectivity, profoundly govern the outcome this process. Hence, when the L-ristosamine-derived, tail-to-tail dimer **19** was subjected to the metathesis protocol the corresponding cyclic neotetra- and hexasaccharides became the major products which were separated by column chromatography (Scheme 6). Their structures were unequivocally



Scheme 6. Macrocyclization of C_2-symmetric *ribo*-configured allyl glycoside **19** by ring closing metathesis. a) **8** (20 mol %), dry C_6H_6, 50 °C, 20 h (64 % for cyclic tetrasaccharide; 16 % for cyclic hexasaccharide); b) PtO_2, H_2, ethyl acetate, RT, 24 h (99 %); c) aq. NaOH (1.0 M)/THF (2:1), RT, 24 h (99 %).

confirmed after hydrogenation of the olefinic double bonds by NMR spectroscopy and mass spectrometry. The highly symmetric character of these spacer-linked macrocycles **34** and **35** is responsible for the fact that only one set of signals for all pyran rings as well as the 1,4-butandiol moieties in the ^1H and ^{13}C NMR spectra is detectable. In addition, the dimeric and trimeric character (based if one assumes that the starting compound **19** is defined as a monomer) and the cyclic structure of aminoglycosides **34** and **35** were confirmed by mass spectrometry (ESI mode). Formation of these macrocycles can be rationalized by assuming that the axial amino substituent at C-3 prevents direct macrocyclization of linear diene **19**. Instead, dimerization and trimerization to linear neotetra- and hexasaccharides occurs prior to macrocyclization.[29] Finally, the target macrocyclic tetrasaccharide **5** was prepared after hydrolytic removal of the four N-protecting groups.

Next, the complex neotetrasaccharide **30** was subjected to the ring-closing metathesis conditions (Scheme 7). This time the reaction proceeded only sluggishly and a complex mixture of products were formed from which the desired cyclization product **36** was isolated after hydrogenation of the olefinic double bond in 22 % yield. The sequence was terminated after removal of the trifluoroacetyl groups under basic conditions which yielded target cyclic aminoglycoside **7**. Noteworthy carbohydrate-based macrocycle **7** contains two special structural features: a) two glycosidic linkages, and b) two linker-based connections, one in the head-to-head, the second one in the tail-to-tail mode. This array of substructures creates a rich



Scheme 7. Macrocyclization of C_2-symmetric tetrasaccharide **30** by ring-closing metathesis. a) **8** (20 mol%, dry C_6H_6, 50 °C, 24 h; b) PtO_2, H_2, ethyl acetate, RT, 18 h (22% for two steps); c) aq. NaOH (0.4 M)/THF (3:1), RT, 18 h (78%).

diversity of novel carbohydrate-based macrocycles that will play a crucial role in studying their affinity to bind to polynucleotides.

In summary, we have described an efficient synthetic route towards novel macrocyclic 1,4-butanediol-linked neooligoaminodeoxysaccharides using two variants of the metathesis olefination. Studies on the biological properties, particularly their affinity to HIV-1 TAR-RNA, of these new neooligosaccharides will reported in due course.

Experimental Section

General techniques: All temperatures quoted are uncorrected. Optical rotations were recorded on a Perkin–Elmer 141 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR, ^{13}C NMR, ^{1}H/^{1}H-, ^{1}H/^{13}C-COSY and HMQC spectra were recorded on a Bruker DPX 200 and a Bruker ARX 400-NMR spectrometer for solutions in $CDCl_3$ using residual $CHCl_3$ as internal standard (δ 7.26) unless otherwise stated. Multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants (J) are quoted in Hz. Chemical shift values of ^{13}C NMR spectra are reported as values in ppm relative to residual $CHCl_3$ (δ 77.0) as internal standard. The multiplicities refer to the resonances in the off-resonance spectra and were elucidated using the distortionless enhancement by polarisation transfer (DEPT) spectral editing technique, with secondary pulses at 90° and 135°. Multiplicities are reported using the following abbreviations: s = singlet (due to quaternary carbon), d = doublet (methine), t = triplet (methylene), and q = quartet (methyl). Mass spectra were obtained using either a LCQ Finnigan instrument using electrospray ionization (ESI) mode or MAT 95 Finnigan (DCI). Ion mass (m/z) signals are reported as values in atomic mass units followed, in parentheses, by the peak intensities relative to the base peak (100%). Combustion analyses were performed by the Institut für Pharmazeutische Chemie, Technische Universität Braunschweig and Institut für Chemie, Humboldt Universität zu Berlin (Germany). All solvents used were of reagent grade and were further dried. Reactions were monitored by TLC on silica gel coated aluminium 60 F_{254} (E. Merck, Darmstadt) and spots were detected either by UV absorption or by charring with H_2SO_4/4-methoxybenzaldehyde in methanol. Flash column chromatography was performed on silica gel 60 (E. Merck, Darmstadt; 35–70 mesh). Sephadex LH-20 (Pharmacia) was employed for preparative column chromatography of final neooligosaccharides. Petroleum ether with a b.p. range of 40–60 was used. Analytical data for 3-azidoglycals **10a–d** can be found in ref. [13].

***tert*-Butyldimethylsilyl 3-azido-2,3,6-trideoxy-β-L-*arabino*-hexopyranoside (12a), *tert*-butyldimethylsilyl-3-azido-2,3,6-trideoxy-β-L-*ribo*-hexopyranoside (12b), *tert*-butyldimethylsilyl 3-azido-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (12c), and *tert*-butyldimethylsilyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (11d)**: A suspension of glycal **9** (4.62 g, 21.6 mmol) in water (40 mL) was heated to 95 °C and stirred for 1 h. After cooling to room temperature sodium azide (2.1 g, 32.4 mmol) and acetic acid (4.3 mL, 3.5 equiv) were added to the resulting solution and the stirring was maintained for 3 h, whereupon TLC (petroleum ether/ethyl acetate 4:1) indicated that the reaction was complete. After the reaction mixture was poured onto a saturated aqueous solution of $NaHCO_3$ the solution was extracted with ethyl acetate. The combined organic layers were dried ($MgSO_4$) and the solvent was removed in vacuo to afford an isomeric mixture of 3-azido pyranoses (4.76 g). This crude material was dissolved in anhydrous 1,2-dichloroethane (40 mL) and imidazole (2.95 g, 43.4 mmol) was added at 0 °C. After 10 min tBuMe$_2$SiCl (5.80 g, 38.5 mmol) was added and the reaction mixture was stirred overnight at room temperature. The solution was extracted with water (2 × 20 mL) and the organic extracts were dried ($MgSO_4$) and concentrated in vacuo to yield an oil (7.44 g). This material was purified by column chromatography (petroleum ether/ethyl acetate 12:1). At this point, only the *ribo*-configured α-silyl isomer of **11d** could be separated from the other three isomers, which were used directly in the next step. Selected analytical data for hexopyranoside **11d** (239 mg, 0.73 mmol, 3.4%): $[\alpha]_D^{22} = -195.3$ (c = 1.10 in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.18 (dd, J = 3.6, 1.5 Hz, 1H; 1-H), 4.57 (dd, J = 9.6, 3.6 Hz, 1H; 4-H), 4.30 (dq, J = 9.6, 6.3 Hz, 1H; 5-H), 4.16 (q, J = 3.6 Hz, 1H; 3-H), 2.11 (s, CH_3CO, 3H), 2.10 (ddd, J = 14.8, 3.6, 1.8 Hz, 1H; 2-H$_{eq}$), 2.01 (dt, J = 14.8, 3.6 Hz, 1H; 2-H$_{ax}$), 1.13 (d, J = 6.3 Hz, 3H; 6-H), 0.92 {s, 9H; Si(CH$_3$)$_2$[C(CH_3)$_3$]}, 0.11, 0.09 {2s, 6H; Si(CH_3)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR (50 MHz; $CDCl_3$, 25 °C): δ = 170.2 (s, *C*OCH$_3$), 90.2 (d, C-1), 73.6 (d, C-4), 61.7 (d, C-5), 55.2 (d, C-3), 34.0 (t, C-2), 25.5 (q, Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]), 20.9 (q, *C*H$_3$CO), 17.9 {s, Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, 17.2 (q, C-6), −4.6, −5.8 {2q, Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{14}H_{27}N_3O_4Si$ (329.5): C 51.04, H 8.26, N 12.75; found C 51.13, H 8.31, N 12.49.

The main fraction including the three isomers (5.8 g, 17.6 mmol) was dissolved in dry methanol (30 mL), and sodium methylate (478 mg, 8.85 mmol) was added. The reaction mixture was stirred at room temperature for 5 h, whereupon TLC (petroleum ether/ethyl acetate 10:1) revealed that the ester hydrolysis was complete. Concentration in vacuo gave a crude material which was purified by column chromatography (petroleum ether/ethyl acetate 10:1).

1st Fraction **12a** (3.06 g, 10.64 mmol, 60.5%); R_f = 0.23 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 4.80 (dd, J = 9.2, 2.0 Hz, 1H; 1-H), 3.39 (ddd, J = 12.6, 9.0, 4.8 Hz, 1H; 3-H), 3.32 (dq, J = 9.0, 6.0 Hz, 1H; 5-H), 3.14 (dt, J = 9.0, 3.6 Hz, 1H; 4-H), 2.23 (d, J = 3.6 Hz, 1H; OH), 2.18 (ddd, J = 13.0, 4.8, 2.2 Hz, 1H; 2-H$_{eq}$), 1.66 (dt, J = 12.6, 9.2 Hz, 1H; 2-H$_{ax}$), 1.32 (d, J = 6.6 Hz, 3H; 6-H), 0.89 {s, 9H; Si(CH$_3$)$_2$[C(CH_3)$_3$]}, 0.12, 0.10 {2s, 6H; Si(CH_3)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{12}H_{25}N_3O_3Si$ (287.4): 50.14, H 8.77, N 14.62; found C 50.22, H 8.55, N 14.43.

2nd Fraction **12b** (1.40 g, 4.87 mmol, 28%); R_f = 0.14 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 4.99 (dd, J = 9.0, 2.0 Hz, 1H; 1-H), 4.05 (q, J = 3.6 Hz, 1H; 3-H), 3.62 (dq, J = 9.4, 6.3 Hz, 1H; 5-H), 3.38 (dt, J = 8.8, 3.6 Hz, 1H; 4-H), 2.10 (ddd, J = 14.0, 3.6, 2.2 Hz, 1H; 2-H$_{eq}$), 1.98 (d, J = 8.5 Hz, 1H; OH), 1.80 (ddd, J = 14.0, 9.0, 3.2 Hz, 1H; 2-H$_{ax}$), 1.27 (d, J = 6.3 Hz, 3H; 6-H), 0.89 {s, 9H; Si(CH$_3$)$_2$[C(CH_3)$_3$]}, 0.10 {2s, 6H; Si(CH_3)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{12}H_{25}N_3O_3Si$ (287.4): C 50.14, H 8.77, N 14.62; found C 50.16, H 8.69, N 14.73.

3rd Fraction **12c** (56 mg, 0.195 mmol, 1.1%); R_f = 0.26 (petroleum ether/ethyl acetate 10:1); $[\alpha]_D^{22} = +68.24$ (c = 1.65 in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.24 (dd, J = 2.4, 1.2 Hz, 1H; 1-H), 3.82 (dq, J = 9.4, 6.2 Hz, 1H; 5-H), 3.77 (ddd, J = 12.6, 9.0, 4.8 Hz, 1H; 3-H), 3.13 (t, J = 9.2 Hz, 1H; 4-H), 2.41 (s, OH, 1H), 2.05 (ddd, J = 12.8, 4.8, 1.6 Hz, 1H; 2-H$_{eq}$), 1.70 (dt, J = 12.6, 3.0 Hz, 1H; 2-H$_{ax}$), 1.25 (d, J = 6.4 Hz, 3H; 6-H),

  0947-6539/02/0812-2722 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

0.90 {s, 9H; $Si(CH_3)_2[C(CH_3)_3]$}, 0.10 {2s, 6H; $Si(CH_3)_2[C(CH_3)_3]$}; elemental analysis calcd (%) for $C_{12}H_{25}N_3O_3Si$ (287.4): C 50.14, H 8.77, N 14.62; found C 50.02, H 8.58, N 14.83.

***tert*-Butyldimethylsilyl 4-*O*-allyl-3-azido-2,3,6-trideoxy-β-L-*arabino*-hexopyranoside (13a)**: NaH (55–65% in oil, 2.5 equiv, 0.73 g) and allyl bromide (1.56 mL, 18.25 mmol) were added to a solution of pyranoside (**12a**) (2.10 g, 7.3 mmol) in anhydrous THF (50 mL). The mixture was stirred at room temperature overnight. Methanol (35 mL) was added and stirring for additional 3 h was continued. The reaction mixture was concentrated under reduced pressure. The residual oil obtained was taken up in water (120 mL) and extraction was carried out with dichloromethane (4 × 20 mL). The combined organic extracts were washed with water and dried ($MgSO_4$). After removal of the solvent under reduced pressure a crude material (2.36 g, 7.21 mmol, 99%) was obtained, which was directly used for the next step without additional purification. **13a**: $R_f = 0.68$ (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 5.95$ (ddt, $J = 17.2$, 10.2, 5.8 Hz, 1H; CH=), 5.29 (dq, $J = 17.2$, 1.7 Hz, 1H; C*H*H′=CH-), 5.20 (dq, $J = 10.2$, 1.6 Hz, 1H; CH*H*′=CH-), 4.76 (dd, $J = 9.4$, 2.0 Hz, 1H; 1-H), 4.16–4.10 (m, 1H; 3-H), 4.29 (ddt, $J = 12.1$, 5.6, 1.3 Hz, 1H; OC*H*H′), 4.14 (ddt, $J = 12.1$, 6.0, 1.2 Hz, 1H; OCH*H*′), 3.32 (dq, $J = 9.2$, 6.4 Hz, 1H; 5-H), 2.89 (t, $J = 9.2$ Hz, 1H; 4-H), 2.13 (ddd, $J = 12.8$, 5.0, 2.0 Hz, 1H; 2-H_{eq}), 1.57 (dt, $J = 12.8$, 9.2 Hz, 1H; 2-H_{ax}), 1.31 (d, $J = 6.2$ Hz, 3H; 6-H), 0.89 {s, 9H; $Si(CH_3)_2[C(CH_3)_3]$}, 0.11, 0.09 {2s, 6H; $Si(CH_3)_2[C(CH_3)_3]$}; ^{13}C NMR (50 MHz; $CDCl_3$, 25 °C): $\delta = 134.2$ (d, =CH), 117.7 (t, CH_2=), 94.3 (d, C-1), 80.9 (d, C-4), 74.0 (t, OCH_2), 72.2 (d, C-5), 62.0 (d, C-3), 39.2 (t, C-2), 25.7 {q, $Si(CH_3)_2[C(CH_3)_3]$}, 18.2 (q, C-6), 18.0 {s, $Si(CH_3)_2[C(CH_3)_3]$}, −4.2, −5.2 {q, $Si(CH_3)_2[C(CH_3)_3]$}.

***tert*-Butyldimethylsilyl 4-*O*-allyl-3-trifluoroacetamido-2,3,6-trideoxy-β-L-arabino-hexopyranoside (14a)**: The azide **13a** (1.14 g, 3.49 mmol) was dissolved in anhydrous diethyl ether (25 mL). To this solution was added lithium aluminium hydride (0.9 g, 23.7 mmol) at 0 °C and stirring was continued for 2.5 h at this temperature. Excess of lithium aluminium hydride was destroyed by dropwise addition of water (1 mL) and 10% NaOH (2 mL). The suspension was filtered with suction and the filter cake was thoroughly washed with diethyl ether. The combined filtrates were concentrated under reduced pressure to afford a syrup which was dried by being taken up in toluene followed by concentration in vacuo. The crude material obtained can be used for the next step without further purification by dissolving it in anhydrous dichloromethane (15 mL) at 0 °C. Triethyl amine (0.7 mL) and trifluoroacetic anhydride (0.73 mL) were added to this solution. The mixture was stirred at room temperature for 0.5 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (petroleum ether/ethyl acetate 15:1) to afford the title compound **14a** (784 mg, 1.97 mmol; 56.4%) as colourless crystals. $R_f = 0.26$ (petroleum ether/ethyl acetate 15:1); m.p. 97–99 °C; $[\alpha]_D^{22} = -8.55$ ($c = 1.14$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta =$ 6.54 (d, $J = 7.2$ Hz, 1H; NH), 5.85 (ddt, $J = 17.2$, 10.4, 5.8 Hz, 1H; CH=), 5.25 (dq, $J = 17.2$, 1.6 Hz, 1H; C*H*H′=CH-), 5.22 (dq, $J = 10.4$, 1.6 Hz, 1H; CH*H*′=CH-), 4.92 (dd, $J = 7.6$, 2.4 Hz, 1H; 1-H), 4.18 (dd, $J = 12.4$, 5.8 Hz, 1H; OC*H*H′), 4.12–4.02 (m, 1H; 3-H), 3.97 (dd, $J = 12.4$, 5.8 Hz, 1H; OCH*H*′), 3.44 (dq, $J = 8.4$, 6.2 Hz, 1H; 5-H), 2.99 (t, $J = 8.4$ Hz, 1H; 4-H), 2.25 (ddd, $J = 12.8$, 4.4, 2.4 Hz, 1H; 2-H_{eq}), 1.62 (ddd, $J = 12.8$, 9.8, 7.6 Hz, 1H; 2-H_{ax}), 1.33 (d, $J = 6.0$ Hz, 3H; 6-H), 0.88 {s, 9H; $Si(CH_3)_2[C(CH_3)_3]$}, 0.11, 0.10 {2s, 6H; $Si(CH_3)_2[C(CH_3)_3]$}; ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 156.7$ (q, *C*OCF_3), 134.2 (d, =CH), 118.5 (t, CH_2=), 116.0 (q, $COCF_3$), 94.1 (d, C-1), 81.5 (d, C-4), 72.9 (t, OCH_2), 72.1 (d, C-5), 50.2 (d, C-3), 38.0 (t, C-2), 25.6 {q, $Si(CH_3)_2[C(CH_3)_3]$}, 18.6 (q, C-6), 18.0 {s, $Si(CH_3)_2[C(CH_3)_3]$}, −4.3, −5.4 {q, $Si(CH_3)_2[C(CH_3)_3]$}; elemental analysis calcd (%) for $C_{17}H_{30}F_3NO_4Si$ (397.5): C 51.37, H 7.61, N 3.52; found C 51.45, H 7.62, N 3.61.

***tert*-Butyldimethlysilyl 4-*O*-allyl-3-azido-2,3,6-trideoxy-β-L-*ribo*-hexopyranoside (13b)**: Freshly prepared dry silver oxide (2.62 g) and allyl iodide (0.5 mL) were added to a solution of pyranoside (**12b**) (992 mg, 3.45 mmol) in dry acetonitrile (20 mL). The mixture was stirred at 50 °C for 20 h under nitrogen. The suspension was filtered through a pad of Celite with suction and the filter cake was washed with ethyl acetate. The combined filtrates were concentrated under reduced pressure to afford a crude oil which was purified by column chromatography (petroleum ether/ethyl acetate 15:1) to give the title compound **13b** (271 mg, 0.83 mmol; 24%). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 5.91$ (ddt, $J = 17.0$, 10.4, 5.8 Hz, 1H; CH=), 5.29 (dq, $J = 17.0$, 1.8 Hz, 1H; C*H*H′=CH-), 5.22 (dq, $J = 10.4$, 1.6 Hz, 1H; CH*H*′=CH-), 4.96 (dd, $J = 9.0$, 1.8 Hz, 1H; 1-H), 4.16–4.10 (m, 1H; 3-H), 4.14 (ddt, $J = 12.4$, 6.0, 1.4 Hz, 1H; OC*H*H′), 4.01 (ddt, $J = 12.4$, 6.0, 1.4 Hz, 1H; OCH*H*′), 3.83 (dq, $J = 9.2$, 6.2 Hz, 1H; 5-H), 3.20 (dd, $J = 9.2$, 3.2 Hz, 1H; 4-H), 1.98 (ddd, $J = 13.8$, 4.5, 2.2 Hz, 1H; 2-H_{eq}), 1.66 (ddd, $J = 13.5$, 9.0, 3.6 Hz, 1H; 2-H_{ax}), 1.27 (d, $J = 6.2$ Hz, 3H; 6-H), 0.88 {s, 9H; $Si(CH_3)_2[C(CH_3)_3]$}, 0.10, 0.09 {2s, 6H; $Si(CH_3)_2[C(CH_3)_3]$}; ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 134.2$ (d, =CH), 117.9 (t, CH_2=), 92.3 (d, C-1), 80.2 (d, C-4), 70.9 (t, OCH_2), 69.2 (d, C-5), 57.4 (d, C-3), 38.1 (t, C-2), 25.8 {3q, $Si(CH_3)_2[C(CH_3)_3]$}, 18.2 (q, C-6), 18.2 {s, $Si(CH_3)_2[C(CH_3)_3]$}, −4.3, −5.3 {2q, $Si(CH_3)_2[C(CH_3)_3]$}; elemental analysis calcd (%) for $C_{15}H_{29}N_3O_3Si$ (327.5): C 55.01, H 8.93, N 12.83; found C 55.11, H 9.02, N 12.74.

***tert*-Butyldimethylsilyl 4-*O*-allyl-3-trifluoroacetamido-2,3,6-trideoxy-β-L-ribo-hexopyranoside (14b)**: Azide **13b** (429 mg, 1.31 mmol) was dissolved in anhydrous THF (18 mL). To this solution was added lithium aluminium hydride (250 mg, 6.59 mmol) at 0 °C and stirring was continued for 2 h at room temperature. Excess of lithium aluminium hydride was destroyed by dropwise addition of water (1 mL) and 10% NaOH (2 mL). The suspension was filtered with suction and the filter cake was thoroughly washed with diethyl ether. The combined filtrates were concentrated under reduced pressure to afford a syrup which was dried by being taken up in toluene followed by concentration in vacuo. The crude material obtained can be used for the next step without further purification by dissolving it in anhydrous dichloromethane (20 mL) at 0 °C. Triethylamine (0.3 mL) and trifluoroacetic anhydride (0.3 mL) were added to the solution. The mixture was stirred at room temperature for 0.5 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (petroleum ether/ethyl acetate 15:1) to afford the title compound **14b** (404 mg, 1.02 mmol; 78%). $R_f = 0.28$ (petroleum ether/ethyl acetate 15:1); $[\alpha]_D^{22} = -15.0$ ($c = 1.22$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 6.60$ (d, $J = 4.8$ Hz, 1H; NH), 5.85 (ddt, $J = 17.0$, 10.4, 5.8 Hz, 1H; CH=), 5.26 (dq, $J = 17.0$, 1.6 Hz, 1H; C*H*H′=CH-), 5.22 (dq, $J = 10.4$, 1.6 Hz, 1H; CH*H*′=CH-), 4.98 (dd, $J = 7.3$, 2.5 Hz, 1H; 1-H), 4.45 (m, 1H; 3-H), 3.99 (dt, $J = 5.8$, 1.4 Hz, 2H; OCH_2), 3.76 (pent., $J = 6.8$ Hz, 1H; 5-H), 3.29 (dd, $J = 7.4$, 4.2 Hz, 1H; 4-H), 2.37 (ddd, $J = 13.8$, 5.8, 2.2 Hz, 1H; 2-H_{eq}), 1.71 (ddd, $J = 13.8$, 7.2, 4.0 Hz, 1H; 2-H_{ax}), 1.34 (d, $J = 6.6$ Hz, 3H; 6-H), 0.88 {s, 9H; $Si(CH_3)_2[C(CH_3)_3]$}, 0.10, 0.09 {2s, 6H; $Si(CH_3)_2[C(CH_3)_3]$}; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 156.8$ (q, *C*OCF_3), 133.6 (d, =CH), 118.3 (t, CH_2=), 116.0 (q, $COCF_3$), 92.6 (d, C-1), 76.4 (d, C-4), 70.2 (t, OCH_2), 69.7 (d, C-5), 45.1 (d, C-3), 35.2 (t, C-2), 25.7 {q, $Si(CH_3)_2[C(CH_3)_3]$}, 19.3 (q, C-6), 18.0 {s, $Si(CH_3)_2[C(CH_3)_3]$}, −4.3, −5.3 {2q, $Si(CH_3)_2[C(CH_3)_3]$}; elemental analysis calcd (%) for $C_{17}H_{30}F_3NO_4Si$ (397.5): C 51.37, H 7.61, N 3.52; found C 51.36, H 7.56, N 3.50.

(*E*,*Z*)-1,4-Bis[*tert*-butyldimethylsilyl 3′-trifluoroacetamido-2′,3′,6′-trideoxy-β-L-*arabino*-hexopyranos-4′-yl]-2-butene-1,4-diol (17), (*E*,*Z*)-1,4-bis[*tert*-butyldimethylsilyl 3′-trifluoroacetamido-2′,3′,6′-trideoxy-β-L-*arabino*-hexopyranos-4′-yl]-1-butene-1,4-diol (18), and *tert*-butyldimethylsilyl (*E*,*Z*)-4-*O*-(1′-propenyl)-3-trifluoroacetamido-2,3,6-trideoxy-β-L-*arabino*-hexopyranoside (16): Allyl ether **14a** (216 mg, 0.544 mmol) was dissolved in dry benzene (10 mL) under nitrogen and the Grubbs catalyst **8** was added in two portions (30 mg, 6.7 mol%; 14 mg, 3.1 mol%). The purple solution was stirred at room temperature for 5 h and after addition of the second portion at 45 °C for 20 h. After removal of the solvent in vacuo the crude material obtained was dissolved in diethyl ethyl (30 mL) and triethylamine (1 mL) and stirred under air for 2 h at room temperature. Concentration of the solution under reduced pressure yielded an oil which was purified by column chromatography (petroleum ether/ethyl acetate 5:1) to yield three fractions.

1st Fraction **17** (150 mg, 0.19 mmol, 70%; *E*/*Z* 6:1, inseparable mixture); $R_f = 0.36$ (petroleum ether/ethyl acetate 4:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) for *E* isomer: $\delta = 6.97$ (d, $J = 8.4$ Hz, 2H; 2 × NH), 5.68 (t, $J = 2.9$ Hz, 2H; 2 × CH=), 4.93 (dd, $J = 7.2$, 2.4 Hz, 2H; 2 × 1-H), 4.14 (br d, $J =$ 12.0 Hz, 2H; 2 × OC*H*H′-CH=), 4.12–4.01 (m, 2H; 2 × 3-H), 3.99 (br d, $J = 12.0$ Hz, 2H; 2 × OCH*H*′-CH=), 3.41 (dq, $J = 8.4$, 6.0 Hz, 2H; 2 × 5-H), 3.03 (t, $J = 8.4$ Hz, 2H; 2 × 4-H), 2.19 (ddd, $J = 13.0$, 4.6, 2.4 Hz, 2H; 2 × 2-H_{eq}), 1.67 (ddd, $J = 13.0$, 10.2, 7.2 Hz, 2H; 2 × 2-H_{ax}), 1.30 (d, $J = 6.0$ Hz, 6H; 2 × 6-H), 0.88 {s, 18H; 2 × $Si(CH_3)_2[C(CH_3)_3]$}, 0.11, 0.10 {2s, 12H; 2 × $Si(CH_3)_2[C(CH_3)_3]$}; ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 156.9$ (q, 2 × *C*OCF_3), 129.5 (d, 2 × =CH), 115.8 (q, 2 × $COCF_3$), 94.1 (d, 2 × C-1), 81.6 (d, 2 × C-4), 72.0 (d, 2 × C-5), 71.6 (t, 2 × -OCH_2), 50.1 (d, 2 × C-3), 37.4 (t,

2 × C-2), 25.6 {q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]}, 18.7 (q, 2 × C-6), 17.9 {s, 2 × Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, −4.3, −5.4 {q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{32}H_{56}F_6N_2O_8Si_2$ (766.96): C 50.11, H 7.36, N 3.65; found C 50.19, H 7.27, N 3.64.

Selected NMR data for *Z* isomer: ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C): δ = 7.53 (d, *J* = 8.4 Hz, 2H; 2 × NH), 5.60 (t, *J* = 4.0 Hz, 2H; 2 × CH=), 4.98 (dd, *J* = 6.8, 2.8 Hz, 2H; 2 × 1-H), 3.08 (t, *J* = 8.0 Hz, 2H; 2 × 4-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 156.7 (q, 2 × *C*OCF$_3$), 129.2 (d, 2 × =CH), 115.8 (q, 2 × CO*C*F$_3$), 82.1 (d, 2 × C-4), 66.8 (t, 2 × OCH$_2$), 49.9 (d, 2 × C-3).

2nd Fraction **18** (17.5 mg, 23 μmol, 8.4%; *E*/*Z* 1.24:1, inseparable mixture); R_f = 0.52 (petroleum ether/ethyl acetate 4:1); ^{1}H NMR of *Z* isomer (400 MHz, CDCl$_3$, 25 °C): δ = 6.85 (d, *J* = 8.6 Hz, 1H; NH), 6.67 (d, *J* = 8.8 Hz, 1H; NH′), 5.96 (d, *J* = 6.2 Hz, 1H; CH=), 4.92 (dd, *J* = 6.3, 3.6 Hz, 1H; 1-H), 4.89 (dd, *J* = 5.7, 3.6 Hz, 1H; 1-H′), 4.32 (dt, *J* = 7.8, 6.4 Hz, 1H; =CHCH$_2$), 4.15 – 4.06 (m, 2H; 3-H, 3-H′), 3.56 – 3.51 (m, 1H; OC*H*H′), 3.48 (dq, *J* = 8.8, 6.4 Hz, 1H; 5-H), 3.44 – 3.39 (m, 1H, OCH*H*′), 3.40 (dq, *J* = 8.8, 5.8 Hz, 1H; 5-H′), 3.27 (t, *J* = 9.0 Hz, 1H; 4-H), 3.00 (t, *J* = 8.6 Hz, 1H; 4-H′), 2.32 – 2.24 (m, 1H; C4-OCH$_2$C*H*H′), 2.19 (ddd, *J* = 12.8, 4.4, 2.4 Hz, 1H; 2-H′$_{eq}$), 2.19 – 2.14 (m, 1H; 2-H$_{eq}$), 2.16 – 2.07 (m, 1H; OCH$_2$CH*H*′), 1.78 (dt, *J* = 12.6, 8.2 Hz, 1H; 2-H$_{ax}$), 1.67 (ddd, *J* = 12.8, 11.2, 8.0 Hz, 1H; 2-H′$_{ax}$), 1.31 (d, *J* = 6.2 Hz, 3H; 6-H′), 1.28 (d, *J* = 6.2 Hz, 3H; 6-H), 0.89, 0.88 {2s, 18H; 2 × Si(CH$_3$)$_2$[C(C*H*$_3$)$_3$]}, 0.12, 0.12, 0.11, 0.10 {4s, 12H; 2 × Si(C*H*$_3$)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR of *Z* isomer (100 MHz, CDCl$_3$, 25 °C): δ = 156.9 (q, 2 × *C*OCF$_3$), 146.3 (d, =CH), 115.7 (q, 2 × CO*C*F$_3$), 102.8 (d, =*C*HCH$_2$), 94.3, 94.3 (d, C-1, C-1′), 83.9 (d, C-4), 82.0 (d, C-4′), 72.1 (d, C-5′), 71.7 (d, C-5), 71.0 (t, OCH$_2$), 50.7, 50.2 (d, C-3, C-3′), 38.5 (t, C-2), 38.3 (t, C-2′), 25.7 {q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]}, 18.7 (q, C-6′), 18.1 (q, C-6), 18.0 {s, 2 × Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, −4.3, −5.3 {q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{32}H_{56}F_6N_2O_8Si_2$ (766.96): C 50.11, H 7.36, N 3.65; found C 50.39, H 7.13, N 3.41.

Selected NMR data for *E* isomer: ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C): δ = 6.99 (d, *J* = 8.4 Hz, 1H; NH), 6.85 (d, *J* = 8.2 Hz, 1H; NH′), 6.14 (d, *J* = 12.4 Hz, 1H; CH=), 4.93 – 4.87 (m, 1H; =CHCH$_2$); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 147.3 (d, =CHO), 103.0 (d, =C*H*CH$_2$), 94.3, 94.0 (d, C-1, C-1′), 82.4 (d, C-4), 81.7 (d, C-4′), 71.6 (d, C-5′ or C-5), 71.0 (t, OCH$_2$), 50.5, 50.2 (d, C-3, C-3′), 37.9 (t, C-2), 37.3 (t, C-2′), 25.7 (q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]), 18.8 (q, C-6′), 18.4 (q, C-6), 18.0 {s, 2 × Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, −4.3, −5.3 {q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}.

3rd Fraction **16** (*E*/*Z* ≅ 1:1, inseparable mixture, 23.8 mg, 60 μmol; 11%); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C): δ = 6.62, 6.58 (2d, *J* = 9.2 Hz, 1H; NH, NH′), 6.04 (dq, *J* = 12.0, 1.6 Hz, 1H; OCH=), 5.93 (dq, *J* = 6.2, 1.6 Hz, 1H; OCH′=), 4.94 (dq, *J* = 12.4, 7.0 Hz, 1H; =CHCH$_3$), 4.92 – 4.84 (m, 2H; 1-H, 1-H′), 4.40 (dq, *J* = 6.8, 6.2 Hz, 1H; =CH′CH$_3$), 4.24 – 4.05 (m, 2H; 3-H, 3-H′), 3.52, 3.47 (2dq, *J* = 8.8, 6.2 Hz, 1H; 5-H, 5-H′), 3.24, 3.19 (2t, *J* = 9.0 Hz, 2H; 4-H, 4-H′), 2.24 (2dt, *J* = 12.8, 4.4 Hz, 2H; 2-H$_{eq}$, 2-H′$_{eq}$), 1.69, 1.63 (2ddd, *J* = 11.6, 8.4, 1.2 Hz, 2H; 2-H$_{ax}$ and 2-H′$_{ax}$), 1.51, 1.47 (2dd, *J* = 7.0, 1.8 Hz, 6H; =CHCH$_3$), 1.29, 1.28 (2d, *J* = 6.3 Hz, 6H; 6-H, 6-H′), 0.89, 0.87 {2s, 18H; 2 × Si(CH$_3$)$_2$[C(C*H*$_3$)$_3$]}, 0.12, 0.11, 0.11, 0.10 {4s, 12H; 2 × Si(C*H*$_3$)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 157.1, 156.8 (2q, *C*OCF$_3$, *C*′OCF$_3$), 146.0, 145.1 (2d, =CH, =C′H), 115.7 (q, *C*OCF$_3$, *C*OC′F$_3$), 102.7, 102.6 (2d, =C′HCH$_3$, =CHCH$_3$), 94.3, 94.2 (2d, C′-1, C-1), 83.5, 82.2 (2d, C′-4, C-4), 71.8, 71.6 (2d, C′-5, C-5), 50.5, 50.5 (2d, C′-3, C-3), 38.7, 38.4 (t, C-2, C′-2), 25.6 (q, Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$], Si(CH$_3$)$_2$[C(*C*′H$_3$)$_3$]), 18.3, 18.1 (2q, C-6, C-6′), 18.0 {s, Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$], Si(CH$_3$)$_2$[*C*′(CH$_3$)$_3$]}, 11.9 (q, *C*H$_3$CH=), 9.0 (q, *C*′H$_3$CH=), −4.3, −5.4 {2q, Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$], Si(*C*′H$_3$)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for $C_{17}H_{30}F_3NO_4Si$ (397.5): C 51.37, H 7.61, N 3.52; found C 51.50, H 7.53, N 3.47.

1,4-Bis[allyl 3′-trifluoroacetamido-2′,3′,6′-trideoxy-α-L-*arabino*-hexopyranos-4′-yl]-1,4-butanediol (15)

Method A: A solution of 10% Pd/C (16 mg) in methanol (8 mL) was stirred under an atmosphere of hydrogen for 30 minutes. To this suspension a solution of the homodimer **17** (64 mg, 82 μmol) in methanol and dichloromethane (1:2, 12 mL) was added. After addition of triethylamine (0.2 mL) the mixture was stirred at room temperature for 10 h, after which time another portion of Pd/C (14 mg) was added to the reaction mixture. Stirring was continued for additional 2 h, whereupon TLC analysis (petroleum ether/ethyl acetate 5:1) indicated that the conversion was complete. The catalyst was removed by filtration and washed (dichloromethane/methanol 10:1). The combined filtrates were concentrated in vacuo and the oil obtained was further purified by flash column chromatography (petroleum ether/ethyl acetate 5:1) to furnish the product (64 mg, 63.9 μmol; 99%) which was used directly for the next reaction. Alternatively, reduction of the olefinic double bond proceeds smoothly using the catalytic system Pd/C (method B).

Method B: PtO_2 (2 mg) was added to a solution of **17** (36 mg, 46 μmol), in ethyl acetate (6 mL). The suspension was stirred under H_2 atmosphere at room temperature for 16 h. The hydrogenation was terminated by addition of Et$_3$N (1 mL), followed by filtration and removal of the solvents in vacuo. The crude material obtained was purified as described above to yield the reduced product (34 mg, 44 μmol; 95%) as a colorless oil. R_f = 0.4 (petroleum ether/ethyl acetate 5:1); $[\alpha]_D^{24} = -3.66$ (*c* = 0.76 in CHCl$_3$); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 6.89 (d, *J* = 8.8 Hz, 2H; 2 × NH), 4.92 (dd, *J* = 7.4, 2.3 Hz, 2H; 2 × 1-H), 4.17 – 4.00 (m, 2H; 2 × 3-H), 3.54 (m, 4H; 2 × OCH$_2$), 3.40 (dq, *J* = 8.7, 6.4 Hz, 2H; 2 × 5-H), 2.96 (t, *J* = 8.4 Hz, 2H; 2 × 4-H), 2.17 (ddd, *J* = 13.1, 4.5, 2.4 Hz, 2H; 2 × 2-H$_{eq}$), 1.66 (ddd, *J* = 13.2, 10.8, 7.2 Hz, 2H; 2 × 2-H$_{ax}$), 1.54 (m, 4H; CH$_2$CH$_2$), 1.30 (d, *J* = 6.6 Hz, 6H; 2 × 6-H), 0.89 {s, 18H; 2 × Si(CH$_3$)$_2$[C(C*H*$_3$)$_3$]}, 0.11, 0.10 {2s, 12H; 2 × Si(C*H*$_3$)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 156.8 (q, 2 × *C*OCF$_3$), 115.8 (q, 2 × CO*C*F$_3$), 94.1 (d, 2 × C-1), 82.4 (d, 2 × C-4), 71.9 (d, 2 × C-5), 71.6 (t, 2 × OCH$_2$), 50.2 (d, 2 × C-3), 37.8 (t, 2 × C-2), 26.7 (t, 2 × *C*H$_2$CH$_2$O), 25.7 {q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]}, 18.7 (q, 2 × C-6), 18.0 {s, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}, −4.3, −5.4 {2q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}; LRMS (ES) (+c): *m*/*z* (%): 791.4 (100) [*M*+Na]$^+$, 1559.9 (52) [2*M*+Na]$^+$.

To a suspension of silyl pyranoside described above (86 mg, 0.11 mmol), powdered molecular sieves in 3 Å in dry dichloromethane (25 mL) at −70 °C under nitrogen was added a catalytic amount of TMSOTf (8.2 μL, 44 μmol). After 15 minutes, freshly distilled allyl alcohol (18 μL, 0.25 mmol) was added and stirring was continued at −60 °C for 0.5 h and −40 °C for 16 h. The reaction mixture was filtered and the filter cake was thoroughly washed with dichloromethane. The combined extracts were washed with an aqueous bicarbonate solution. After extraction of the aqueous phase with ethyl acetate, the combined organic extracts were dried (MgSO$_4$) and concentrated under reduced pressure. The crude material obtained was purified by column chromatography (petroleum ether/ethyl acetate 4:1) to yield the desired product **15** (62 mg, 0.10 mmol, 89.3%) as colorless crystals. R_f = 0.26 (petroleum ether/ethyl acetate 3:1); m.p. 212 – 214 °C; $[\alpha]_D^{23} = -111.0$ (*c* = 0.77 in CHCl$_3$/MeOH 2:1); ^{1}H NMR (200 MHz, CDCl$_3$/CD$_3$OD, 25 °C): δ = 5.82 (dddd, *J* = 17.0, 10.2, 6.0, 5.0 Hz, 2H; 2 × CH=), 5.27 (dq, *J* = 17.0, 1.8 Hz, 2H; 2 × C*H*H′=CH-), 5.22 (dq, *J* = 10.2, 1.6 Hz, 2H; 2 × CH*H*′=CH-), 4.89 (d, *J* = 2.6 Hz, 2H; 2 × 1-H), 4.24 (ddd, *J* = 12.0, 8.2, 4.8 Hz, 2H; 2 × 3-H), 4.06 (ddt, *J* = 12.8, 5.0, 1.6 Hz, 2H; 2 × OC*H*H′), 3.86 (ddt, *J* = 12.8, 6.0, 1.4 Hz, 2H; 2 × OCH*H*′), 3.69 (dq, *J* = 9.2, 6.3 Hz, 2H; 2 × 5-H), 3.55 – 3.44 (m, 2H; 2 × OC*H*H′), 3.44 – 3.34 (m, 2H; 2 × OCH*H*′), 2.89 (t, *J* = 9.6 Hz, 2H; 2 × 4-H), 1.95 (ddd, *J* = 12.8, 4.9, 1.2 Hz, 2H; 2 × 2-H$_{eq}$), 1.78 (dt, *J* = 12.8, 3.4 Hz, 2H; 2 × 2-H$_{ax}$), 1.44 (m, 4H; CH$_2$CH$_2$), 1.19 (d, *J* = 6.0 Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 156.8 (q, 2 × *C*OCF$_3$), 133.8 (d, =CH), 117.0 (t, CH$_2$=), 116.0 (q, 2 × CO*C*F$_3$), 95.2 (d, 2 × C-1), 82.3 (d, 2 × C-4), 72.2 (t, 2 × OCH$_2$), 67.6 (d, 2 × C-5), 67.6 (t, 2 × OCH$_2$), 48.1 (d, 2 × C-3), 35.1 (t, 2 × C-2), 26.8 (t, 2 × *C*H$_2$CH$_2$O), 17.9 (q, 2 × C-6); elemental analysis calcd (%) for $C_{26}H_{38}F_6N_2O_8$ (620.6) C 50.32, H 6.17, N 4.51; found C 50.55, H 6.01, N 4.72.

1,4-Bis[*tert*-butyldimethylsilyl 3′-trifluoroacetamido-2′,3′,6′-trideoxy-β-L-ribo-hexopyranos-4′-yl]-2-butene-1,4-diol (20): Allyl ether **14b** (105 mg, 0.264 mmol) was dissolved in dry benzene (20 mL) under nitrogen and the Grubbs catalyst **8** was added in two portions (19 mg, 8.7 mol%; 10 mg, 4.4 mol%). The purple solution was stirred at room temperature for 2 h and after addition of the second portion at 40 °C for 20 h. After removal of the solvent in vacuo the crude material obtained was dissolved in diethyl ethyl (30 mL) and triethylamine (1 mL) and stirred under air for 2 h at room temperature. Concentration of the solution under reduced pressure yielded an oil which was purified by column chromatography (petroleum ether/ethyl acetate 7:1 to 4:1) to yield the desired dimer **20** (63 mg, 82 μmol, 62%; *E*/*Z* >20:1) as a colourless oil. R_f = 0.30 (petroleum ether/ethyl acetate 10:1); $[\alpha]_D^{22} = -8.4$ (*c* = 0.81 in CHCl$_3$); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C): δ = 6.54 (d, *J* = 5.8 Hz, 2H; 2 × NH), 5.72 (m, 2H; 2 × CH=), 4.98 (dd, *J* = 7.2, 2.2 Hz, 2H; 2 × 1-H), 4.46 (m, 2H; 2 × 3-H), 3.99 – 3.97 (m, 4H; 2 × OCH$_2$), 3.74 (pent, *J* = 6.6 Hz, 2H; 2 × 5-H), 3.26 (dd, *J* = 7.0, 4.2 Hz, 2H; 2 × 4-H), 2.33 (ddd, *J* = 13.8, 5.8, 2.4 Hz, 2H; 2 × 2-H$_{eq}$), 1.71 (ddd, *J* = 13.6, 7.2, 4.2 Hz, 2H; 2 × 2-H$_{ax}$), 1.34 (d, *J* = 6.6 Hz, 6H;

0947-6539/02/0812-2724 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

2 × 6-H), 0.88 {s, 18H; 2 × Si(CH$_3$)$_2$[C(C*H*$_3$)$_3$]{, 0.10, 0.09 {2s, 12H; 2 × Si(C*H*$_3$)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 156.8 (q, 2 × *C*OCF$_3$), 129.1 (d, 2 × =CH), 116.0 (q, 2 × CO*C*F$_3$), 92.5 (d, 2 × C-1), 77.0 (d, 2 × C-4), 69.6 (d, 2 × C-5), 69.0 (t, 2 × OCH$_2$), 45.0 (d, 2 × C-3), 35.3 (t, 2 × C-2), 25.6 {q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]}, 19.2 (q, 2 × C-6), 18.0 {s, 2 × Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, −4.3, −5.3 {q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}; elemental analysis calcd (%) for C$_{26}$H$_{38}$F$_6$N$_2$O$_8$ (620.6): C 50.32, H 6.17, N 4.51; found C 50.44, H 6.10, N 4.69.

1,4-Bis(allyl 3′-trifluoroacetamido-2′,3′,6′-trideoxy-α-L-*ribo*-hexopyranos-4′-yl)-1,4-butanediol (19): To a solution of homodimer **20** (101 mg, 0.13 μmol), in dichloromethane/methanol (3:1, 8 mL) was added PtO$_2$ (4 mg). The suspension was stirred under H$_2$ atmosphere at room temperature for 22 h. The hydrogenation was terminated by addition of Et$_3$N (1 mL), followed by filtration and removal of the solvents in vacuo. The crude material obtained was purified by flash column chromatography (petroleum ether/ethyl acetate 6:1) to furnish the desired product [88 mg, 0.11 mmol; 87%; R_f = 0.26 (petroleum ether/ethyl acetate 10:1)] which could directly subjected for the next reaction. Selected analytical data for the product: $[\alpha]_D^{23} = -6.7$ (c = 0.47 in CHCl$_3$); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 6.54 (d, J = 5.8 Hz, 2H; 2 × NH), 4.95 (dd, J = 7.6, 2.0 Hz, 2H; 2 × 1-H), 4.45 (pent., J = 4.8 Hz, 2H; 2 × 3-H), 3.70 (dq, J = 7.4, 6.4 Hz, 2H; 2 × 5-H), 3.48–3.38 (m, 4H; 2 × OCH$_2$), 3.17 (dd, J = 7.4, 4.2 Hz, 2H; 2 × 4-H), 2.34 (ddd, J = 13.8, 5.4, 2.2 Hz, 2H; 2 × 2-H$_{eq}$), 1.70 (ddd, J = 13.8, 7.8, 4.0 Hz, 2H; 2 × 2-H$_{ax}$), 1.57 (m, 4H; CH$_2$CH$_2$), 1.32 (d, J = 6.6 Hz, 6H; 2 × 6-H), 0.88 {s, 18H; 2 × Si(CH$_3$)$_2$[C(C*H*$_3$)$_3$]}, 0.08, 0.09 {2s, 12H; 2 × Si(C*H*$_3$)$_2$[C(CH$_3$)$_3$]}; ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 157.3 (q, 2 × *C*OCF$_3$), 115.7 (q, 2 × CO*C*F$_3$), 92.6 (d, 2 × C-1), 77.5 (d, 2 × C-4), 69.6 (d, 2 × C-5), 68.9 (t, 2 × OCH$_2$), 45.2 (d, 2 × C-3), 35.3 (t, 2 × C-2), 26.4 (t, 2 × *C*H$_2$CH$_2$O), 25.7 {q, 2 × Si(CH$_3$)$_2$[C(*C*H$_3$)$_3$]}, 19.1 (q, C-6), 18.0 {s, 2 × Si(CH$_3$)$_2$[*C*(CH$_3$)$_3$]}, −4.3, −5.3 {2q, 2 × Si(*C*H$_3$)$_2$[C(CH$_3$)$_3$]}.

To a suspension of silyl pyranoside described above (97 mg, 0.12 mmol), and powdered molecular sieves (3 Å) in dry dichloromethane (14 mL) at −70 °C under nitrogen was added a catalytic amount of TMSOTf (8.2 μL, 44 μmol). After 15 minutes, freshly distilled allyl alcohol (21 μL, 0.29 mmol) was added and stirring was continued at −60 °C for 0.5 h and −40 °C for 16 h. The reaction mixture was filtered and the filter cake was thoroughly washed with dichloromethane. The combined extracts were washed with an aqueous bicarbonate solution. After extraction of the aqueous phase with ethyl acetate, the combined organic extracts were dried (MgSO$_4$) and concentrated under reduced pressure. The crude material obtained was purified by column chromatography (petroleum ether/ethyl acetate 5:1) to yield the desired product **19** (69 mg, 0.11 mmol, 88.1%).R_f = 0.18 (petroleum ether/ethyl acetate 4:1); $[\alpha]_D^{22} = -103.1$ (c = 1.54 in CHCl$_3$); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 7.87 (d, J = 8.8 Hz, 2H; 2 × NH), 5.89 (ddt, J = 17.0, 10.4, 5.8 Hz, 2H; 2 × CH=), 5.27 (dq, J = 17.0, 1.8 Hz, 2H; 2 × C*H*H′=CH-), 5.22 (dq, J = 10.4, 1.6 Hz, 2H; 2 × CH*H*′=CH-), 4.89 (t, J = 2.2 Hz, 2H; 2 × 1-H), 4.61 (m, 2H; 2 × 3-H), 4.20 (ddt, J = 12.4, 5.4, 1.3 Hz, 2H; 2 × OCHOC*H*H′), 3.94 (ddt, J = 12.4, 6.0, 1.3 Hz, 2H; 2 × OCHOCH*H*′), 3.84–3.72 (m, 2H; 2 × OC*H*H′), 3.72 (dq, J = 9.6, 6.0 Hz, 2H; 2 × 5-H), 3.34–3.22 (m, 2H; 2 × OCH*H*′), 3.04 (dd, J = 9.6, 4.0 Hz, 2H; 2 × 4-H), 1.99–1.96 (m, 4H; 2 × 2-H$_{eq}$, 2 × 2-H$_{ax}$), 1.51 (m, 4H; CH$_2$CH$_2$), 1.26 (d, J = 6.0 Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 156.8 (q, 2 × *C*OCF$_3$), 133.2 (d, =CH), 117.8 (t, CH$_2$=), 116.0 (q, 2 × CO*C*F$_3$), 96.0 (d, 2 × C-1), 78.8 (d, 2 × C-4), 69.4 (t, 2 × OCH$_2$), 68.3 (t, 2 × OCHO*C*H$_2$), 63.4 (d, 2 × C-5), 43.5 (d, 2 × C-3), 32.8 (t, 2 × C-2), 26.1 (t, 2 × *C*H$_2$CH$_2$O), 17.9 (q, 2 × C-6); elemental analysis calcd (%) for C$_{26}$H$_{38}$F$_6$N$_2$O$_8$ (620.6): C 50.32, H 6.17, N 4.51; found C 50.44, H 6.10, N 4.69.

Allyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-α,β-L-*arabino*-hexopyranoside (21a, 21b), and allyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-α,β-L-*ribo*-hexopyranoside (21c, 21d)

Method A (using Dowex 50, H$^+$ form): A suspension of Dowex 50 (H$^+$) (1 g) in freshly distilled allyl alcohol (10 mL) was heated under reflux for 30 minutes, filtered and the resin was washed with absolute allyl alcohol (5 mL). This resin was added to a solution of the crude material (**10a–d**) (1.17 g, 5.4 mmol) in absolute allyl alcohol (10 mL). The suspension was stirred at 90 °C for 1 h. The mixture was filtered with suction while hot and washed with dichloromethane. After concentration of the combined filtrates in vacuo the crude product was subsequently purified by column chromatography (petroleum ether/ethyl acetate 10:1) to afford the title compounds **21a–d** with slightly lower yield (0.55 g, 2.16 mmol, 40%) compared to method B.

Method B (using catalyst montmorillonite K 10): Dry pyridine (12 mL) and acetic anhydride (16.8 mL) were added to a solution of the crude mixture of 3-azido pyranoses **10a–d** (17.1 g, 79.5 mmol) in anhydrous dichloromethane (100 mL). The reaction mixture was stirred at room temperature for 10 h. Ice water was added and the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic phases were dried (MgSO$_4$) and concentrated under reduced pressure to yield an oil (19.2 g) which was directly used for the next step. To a solution of a portion of this material (9.54 g, 37.1 mmol) in anhydrous benzene (80 mL) was added freshly distilled allyl alcohol (6 mL) and montmorillonite K 10 (18 g). The suspension was vigorously stirred at 110 °C overnight. The clay was removed by filtration and washed with dichloromethane (2 × 20 mL). The combined organic filtrates were concentrated under reduced pressure to afford an oil which was purified by column chromatography (petroleum ether/ethyl acetate 10:1) to yield four fractions of allyl glycosides **21a–c** (6.16 g, 24.1 mmol, 65%).

1st Fraction: Allyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**21a**) (4.64 g, 18.2 mmol, 49%). R_f = 0.55 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 5.89 (ddt, J = 17.2, 10.4, 5.4 Hz, 1H; CH=), 5.28 (dq, J = 17.2, 1.6 Hz, 2H; C*H*H′=CH-), 5.23 (dq, J = 10.4, 1.2 Hz, 1H; CH*H*′=CH-), 4.83 (d, J = 2.8 Hz, 1H; 1-H), 4.60 (t, J = 9.6 Hz, 1H; 4-H), 4.07 (ddt, J = 12.8, 5.2, 1.5 Hz, 1H; OC*H*H′), 3.88 (ddt, J = 12.8, 5.2, 1.5 Hz, 1H; OCH*H*′), 3.90–3.74 (m, 1H; 3-H), 3.74 (dq, J = 9.6, 6.2 Hz, 1H; 5-H), 2.10 (ddd, J = 13.2, 5.2, 1.2 Hz, 1H; 2-H$_{eq}$), 2.06 (s, 3H; CH$_3$CO), 1.67 (ddd, J = 13.2, 12.4, 3.6 Hz, 1H; 2-H$_{ax}$), 1.09 (d, J = 6.2 Hz, 3H; 6-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 170.0 (s, CH$_3$CO), 133.7 (d, =CH), 117.4 (t, CH$_2$=), 95.4 (d, C-1), 74.5 (d, C-4), 67.9 (t, OCH$_2$), 65.9 (d, C-5), 57.6 (d, C-3), 35.1 (t, C-2), 20.8 (q, CH$_3$CO), 17.4 (q, C-6); elemental analysis calcd (%) for C$_{11}$H$_{17}$N$_3$O$_4$ (255.3): C 51.76, H 6.71, N 16.46; found C 51.69, H 6.80, N 16.52.

2nd Fraction: Allyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (**21c**) (0.85 g, 3.34 mmol, 9%). R_f = 0.33 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 5.89 (ddt, J = 17.2, 10.2, 6.0 Hz, 1H; CH=), 5.31 (dq, J = 17.2, 1.6 Hz, 2H; C*H*H′=CH-), 5.17 (dq, J = 10.2, 1.5 Hz, 1H; CH*H*′=CH-), 4.81 (dd, J = 3.6, 1.5 Hz, 1H; 1-H), 4.64 (dd, J = 9.6, 3.6 Hz, 1H; 4-H), 4.20 (dq, J = 9.4, 6.4 Hz, 1H; 5-H), 4.17 (ddt, J = 13.4, 6.0, 1.2 Hz, 1H; OC*H*H′), 4.15–4.07 (m, 1H; 3-H), 3.96 (ddt, J = 13.4, 6.0, 1.2 Hz, 1H; OCH*H*′), 2.13 (m, 1H; 2-H$_{eq}$), 2.11 (s, 3H; CH$_3$CO), 2.08 (m, 1H; 2-H$_{ax}$), 1.16 (d, J = 6.2 Hz, 3H; 6-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 170.1 (s, CH$_3$CO), 134.0 (d, =CH), 117.0 (t, CH$_2$=), 94.4 (d, C-1), 73.9 (d, C-4), 68.1 (t, OCH$_2$), 61.8 (d, C-5), 55.6 (d, C-3), 32.7 (t, C-2), 20.7 (q, CH$_3$CO), 17.2 (q, C-6); elemental analysis calcd (%) for C$_{11}$H$_{17}$N$_3$O$_4$ (255.3): C 51.76, H 6.71, N 16.46; found C 51.79, H 6.54, N 16.57.

3rd Fraction: Allyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-β-L-*ribo*-hexopyranoside (**21b**) (0.66 g, 2.6 mmol, 7%). R_f = 0.47 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 5.89 (ddt, J = 17.2, 10.2, 6.0 Hz, 1H; CH=), 5.27 (dq, J = 17.2, 1.6 Hz, 2H; C*H*H′=CH-), 5.18 (dq, J = 10.2, 1.5 Hz, 1H; CH*H*′=CH-), 4.74 (dd, J = 8.8, 2.2 Hz, 1H; 1-H), 4.64 (dd, J = 9.4, 3.6 Hz, 1H; 4-H), 4.32 (ddt, J = 12.8, 5.2, 1.5 Hz, 1H; OC*H*H′), 4.17 (q, J = 3.6, 1H; 3-H), 4.02 (ddt, J = 12.8, 5.2, 1.5 Hz, 1H; OCH*H*′), 3.94 (dq, J = 9.4, 6.4 Hz, 1H; 5-H), 2.12 (s, 3H; CH$_3$CO), 2.05 (ddd, J = 14.0, 3.6, 2.2 Hz, 1H; 2-H$_{eq}$), 1.83 (ddd, J = 14.0, 8.8, 3.6 Hz, 1H; 2-H$_{ax}$), 1.23 (d, J = 6.4 Hz, 3H; 6-H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C, TMS): δ = 170.5 (s, CH$_3$CO), 134.3 (d, =CH), 118.0 (t, CH$_2$=), 97.0 (d, C-1), 74.7 (d, C-4), 70.1 (t, OCH$_2$), 68.5 (d, C-5), 58.1 (d, C-3), 35.7 (t, C-2), 21.1 (q, CH$_3$CO), 18.2 (q, C-6); elemental analysis calcd (%) for C$_{11}$H$_{17}$N$_3$O$_4$ (255.3): C 51.76, H 6.71, N 16.46; found C 51.58, H 6.91, N 16.66.

Allyl 3-trifluoroacetamido-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (22c): Allyl pyranoside (**21c**) (421 mg, 1.65 mmol) was dissolved in anhydrous diethyl ether (20 mL) and after cooling to 0 °C, lithium aluminium hydride (250 mg, 4 equiv) was added. After stirring for 2 h the reduction of the azide as well as the acyl moieties were completed. Excess of the hydride was destroyed by dropwise addition of water (1 mL), 10% aqueous NaOH (2 mL) and again water (3 mL). The suspension was filtered through a pad of Celite with suction and the filtrate was concentrated in vacuo. The crude material obtained was taken up in ethyl acetate and filtered again. The filtrate was concentrated under reduced pressure. The crude oil obtained

was dissolved in anhydrous dichloromethane (20 mL) at 0 °C and dry triethylamine (0.5 mL), and subsequently trifluoroacetic anhydride (0.5 mL) were added. The reaction mixture was stirred at room temperature for 1 h. Removal of the solvent in vacuo afforded a crude product, which was dissolved in allyl alcohol (8 mL). The mixture was stirred at room temperature for 2 h and concentrated under reduced pressure. Purification of the crude oil by flash chromatography (petroleum ether/ethyl acetate 5:1) to afford the title compound **22c** (136 mg, 0.48 mmol, 29% for two steps). $R_f = 0.34$ (petroleum ether/ethyl acetate 5:1); $[\alpha]_D^{23} = -44.2$ ($c = 1.2$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.15$ (d, $J = 6.8$ Hz, 1H; NH), 5.89 (ddt, $J = 17.0$, 10.2, 5.8 Hz, 1H; CH=), 5.28 (dq, $J = 17.0$, 1.6 Hz, 2H; C*H*H′=CH-), 5.23 (dq, $J = 10.2$, 1.2 Hz, 1H; CH*H*′=CH-), 4.91 (d, $J = 1.7$ Hz, 1H; 1-H), 4.45 (m, 1H; 3-H), 4.21 (ddt, $J = 12.2$, 5.6, 1.3 Hz, 1H; OC*H*H′), 3.96 (ddt, $J = 12.4$, 5.8, 1.2 Hz, 1H; OCH*H*′), 3.73 (dq, $J = 9.6$, 6.0 Hz, 1H; 5-H), 3.52 (dd, $J = 9.6$, 3.8 Hz, 1H; 4-H), 2.66 (br s, 1H; OH), 2.10 (dt, $J = 14.8$, 3.7 Hz, 1H; 2-H_{eq}), 1.95 (ddd, $J = 14.8$, 3.2, 1.6 Hz, 1H; 2-H_{ax}), 1.28 (d, $J = 6.0$ Hz, 3H; 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 158.5$ (q, *C*OCF$_3$), 133.1 (d, =CH), 118.0 (t, CH_2=), 115.9 (q, CO*C*F$_3$), 95.8 (d, C-1), 72.7 (d, C-4), 68.3 (t, OCH_2), 64.3 (d, C-5), 48.0 (d, C-3), 32.6 (t, C-2), 17.5 (q, C-6); elemental analysis calcd (%) for $C_{11}H_{16}F_3NO_4$ (283.2): C 46.64, H 5.69, N 4.95; found C 46.51, H 5.71, N 4.88.

1,4-Di-(3′-trifluoroacetamido-2′,3′,6′-trideoxy-α-L-*ribo*-hexopyranosyl)-2-butene-1,4-diol (25), and 1-propenyl (3′-trifluoroacetamido-2′,3′,6′-trideoxy-α-L-*ribo*-hexopyranoside) (24): Allyl ether **22c** (162 mg, 0.57 mmol) was dissolved in dry benzene (16 mL) under nitrogen and the Grubbs catalyst **8** (39 mg, 8.3 mol%) was added in one portion. The purple solution was stirred at 50 °C for 10 h. After removal of the solvent in vacuo the crude material obtained was dissolved in diethyl ethyl (30 mL) and triethylamine (1 mL) and stirred under air for 2 h at room temperature. Concentration of the solution under reduced pressure yielded an oil which was purified by column chromatography (petroleum ether/ethyl acetate 2:1) to yield the desired homodimer **25** (30 mg, 56 μmol, 20%; only *E* isomer), rearranged starting allyl glycoside **24** (89 mg, 0.31 mmol, 55%; *E*/*Z* 1:3.8) and traces of rearranged dimer **26**.

1st Fraction: Compound **25** as a colourless oil. $R_f = 0.10$ (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{23} = -33.4$ ($c = 1.34$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.11$ (d, $J = 7.6$ Hz, 2H; 2 × NH), 5.83 (t, $J = 3.1$ Hz, 2H; 2 × CH=), 4.92 (d, $J = 2.2$ Hz, 2H; 2 × 1-H), 4.80 (m, 2H; 2 × 3-H), 4.29 – 4.19 (2m, $J = 12.2$ Hz, 2H; 2 × OC*H*H′), 4.05 – 3.93 (2d, $J = 12.2$ Hz, 2H; 2 × OCH*H*′), 3.72 (dq, $J = 9.6$, 6.2 Hz, 2H; 2 × 5-H), 3.54 (ddd, $J = 9.6$, 3.4, 2.6 Hz, 2H; 2 × 4-H), 2.59 (d, $J = 2.5$ Hz, 2H; 2 × OH), 2.10 (dt, $J = 14.8$, 3.8 Hz, 2H; 2 × 2-H_{eq}), 1.98 (ddd, $J = 14.8$, 3.2, 1.4 Hz, 2H; 2 × 2-H_{ax}), 1.30 (d, $J = 6.4$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 158.5$ (q, 2 × CF_3CO), 128.7 (d, 2 × CH=), 116.0 (q, 2 × *C*F$_3$CO), 95.8 (d, 2 × C-1), 72.9 (d, 2 × C-4), 66.9 (t, 2 × OCH_2), 64.4 (d, 2 × C-5), 48.0 (d, 2 × C-3), 32.5 (t, 2 × C-2), 17.5 (q, 2 × C-6); elemental analysis calcd (%) for $C_{20}H_{28}F_6N_2O_8$ (538.4): C 44.61, H 5.24, N 5.20; found C 44.53, H 5.29, N 5.08.

2nd Fraction: Compound **24** (inseparable mixture of *E*/*Z* isomers). ^{1}H NMR of *Z* isomer (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.87$ (d, $J = 6.8$ Hz, 1H; NH), 6.13 (dq, $J = 6.2$, 1.8 Hz, 1H; OCH=), 5.12 – 5.08 (m, 1H; 1-H), 4.65 (pent, $J = 6.8$ Hz, 1H; =C*H*CH$_3$), 4.52 (m, 1H; 3-H), 3.75 (dq, $J = 9.8$, 6.0 Hz, 1H; 5-H), 3.57 (dd, $J = 9.6$, 4.0 Hz, 1H; 4-H), 2.53 (br s, 1H; OH), 2.10 (dt, $J = 12.0$, 4.0 Hz, 1H; 2-H_{eq}), 2.09 (ddd, $J = 12.0$, 3.4, 1.8 Hz, 1H; 2-H_{ax}), 1.60 (dd, $J = 7.0$, 1.8 Hz, 3H; =CHC*H*$_3$), 1.29 (d, $J = 6.0$ Hz, 3H; 6-H); ^{13}C NMR of *Z* isomer (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 158.5$ (q, *C*OCF$_3$), 141.3 (d, =CHO), 115.9 (q, CO*C*F$_3$), 104.0 (d, =*C*HCH$_3$), 96.8 (d, C-1), 72.8 (d, C-4), 64.6 (d, C-5), 47.8 (d, C-3), 32.2 (t, C-2), 17.5 (q, C-6), 9.0 (q, *C*H$_3$CH=); selected NMR data for *E* isomer: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.00$ (d, $J = 6.8$ Hz, 1H; NH), 6.18 (dq, $J = 14.0$, 1.6 Hz, 1H; =CHO), 1.58 (dd, $J = 6.8$, 1.6 Hz, 3H; =CHC*H*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 105.5$ (d, =*C*HCH$_3$), 96.3 (d, C-1), 12.3 (q, *C*H$_3$CH=); elemental analysis calcd (%) for $C_{11}H_{16}F_3NO_4$ (283.2): C 46.64, H 5.69, N 4.95; found C 46.44, H 5.81, N 4.82.

Allyl 4-*O*-acetyl-3-trifluoroacetamido-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (27): Triethylamine (0.34 mL, 2 equiv), acetic anhydride (0.23 mL, 2 equiv), and a catalytic amount of 4-DMAP (5 mg) were added under nitrogen to a solution of alcohol **22** (344 mg, 1.22 mmol) in dichloromethane (12 mL). The reaction mixture was stirred at room temperature for 1 h and concentrated under reduced pressure. The crude material was purified by column chromatography (petroleum ether/ethyl acetate 4:1) to yield the desired acetate **27** (366 mg, 1.13 mmol, 92%). $R_f = 0.28$ (petroleum ether/ethyl acetate 4:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.04$ (d, $J = 7.0$ Hz, 1H; NH), 5.89 (ddt, $J = 17.0$, 10.2, 5.8 Hz, 1H; CH=), 5.28 (dq, $J = 17.0$, 1.6 Hz, 2H; C*H*H′=CH-), 5.23 (dq, $J = 10.2$, 1.2 Hz, 1H; CH*H*′=CH-), 4.92 (t, $J = 3.0$ Hz, 1H; 1-H), 4.58 (m, 1H; 3-H), 4.56 (dq, $J = 10.0$, 3.8 Hz, 1H; 4-H), 4.21 (ddt, $J = 12.6$, 5.4, 1.2 Hz, 1H; OC*H*H′), 3.96 (ddt, $J = 12.6$, 5.8, 1.2 Hz, 1H; OCH*H*′), 3.89 (dq, $J = 10.0$, 6.2 Hz, 1H; 5-H), 2.10 (dt, $J = 14.8$, 3.7 Hz, 1H; 2-H_{eq}), 1.96 (s, 3H; C*H*$_3$CO), 1.95 (dq, $J = 14.8$, 1.3 Hz, 1H; 2-H_{ax}), 1.18 (d, $J = 6.0$ Hz, 3H; 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 170.1$ (s, *C*OCH$_3$), 157.1 (q, *C*OCF$_3$), 132.9 (d, =CH), 118.1 (t, CH_2=), 115.9 (q, CO*C*F$_3$), 96.0 (d, C-1), 72.3 (d, C-4), 68.4 (t, OCH_2), 61.8 (d, C-5), 44.6 (d, C-3), 32.4 (t, C-2), 20.5 (q, CO*C*H$_3$), 17.4 (q, C-6); elemental analysis calcd (%) for $C_{13}H_{18}F_3NO_5$ (325.3): C 48.00, H 5.58, N 4.31; found C 48.03, H 5.60, N 4.27.

1,4-Di-(3′-trifluoroacetamido-4′-*O*-acetyl-2′,3′,6′-trideoxy-α-L-*ribo*-hexopyranosyl)-2-butene-1,4-diol (28): Allyl ether **27** (96 mg, 0.30 mmol) was dissolved in dry benzene (18 mL) under nitrogen and the Grubbs catalyst **8** was added in two portions (13 mg, 5.4 mol% and 9 mg, 3.7 mol%). The purple solution was stirred at room temperature for 2 h and after addition of the second portion of catalyst 50 °C for 10 h. After removal of the solvent in vacuo the crude material obtained was dissolved in diethyl ether (30 mL) and triethylamine (1 mL) and stirred under air for 2 h at room temperature. Concentration of the solution under reduced pressure yielded an oil which was purified by column chromatography (petroleum ether/ethyl acetate 5:1 then switched to petroleum ether/ethyl acetate 2:1) to yield the desired homodimer **28** as a colorless oil (43 mg, 0.69 mmol, 46%; *E*/*Z* ratio 2.5:1) and traces of rearranged dimer **29**. Compound **28**: $R_f = 0.12$ (petroleum ether/ethyl acetate 5:1); inseparable mixture of *E*/*Z* isomers); ^{1}H NMR of *E* isomer (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.02$ (d, $J = 8.0$ Hz, 2H; 2 × NH), 5.86 (t, $J = 3.1$ Hz, 2H; 2 × CH=), 4.95 (d, $J = 2.4$ Hz, 2H; 2 × 1-H), 4.62 (m, 2H; 2 × 3-H), 4.56 (dd, $J = 9.8$, 4.0 Hz, 2H; 2 × 4-H), 4.33 – 4.20 (m, 2H; 2 × OC*H*H′), 4.05 – 3.93 (m, 2H; 2 × OCH*H*′), 3.92 (dq, $J = 9.6$, 6.0 Hz, 2H; 2 × 5-H), 2.14 (dt, $J = 14.8$, 3.4 Hz, 2H; 2 × 2-H_{eq}), 1.99 (s, 6H; 2 × CH_3CO), 1.96 (ddd, $J = 14.6$, 2.4, 1.2 Hz, 2H; 2 × 2-H_{ax}), 1.22 (d, $J = 6.2$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 170.2$ (s, 2 × CH_3CO), 156.9 (q, 2 × CF_3CO), 128.7 (d, 2 × CH=), 116.0 (q, 2 × *C*F$_3$CO), 96.1 (d, 2 × C-1), 72.2 (d, 2 × C-4), 67.1 (t, 2 × OCH_2), 61.9 (d, 2 × C-5), 44.7 (d, 2 × C-3), 32.5 (t, 2 × C-2), 20.6 (q, 2 × CH_3CO), 17.3 (q, 2 × C-6); selected NMR data of *Z* isomer: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.79$ (t, $J = 4.2$ Hz, 2H; 2 × CH=), 1.21 (d, $J = 6.0$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 170.1$ (s, 2 × CH_3CO), 157.0 (q, 2 × CF_3CO), 128.9 (d, 2 × CH=), 116.0 (q, 2 × *C*F$_3$CO), 96.0 (d, 2 × C-1), 72.2 (d, 2 × C-4), 62.5 (t, 2 × OCH_2), 62.0 (d, 2 × C-5), 44.6 (d, 2 × C-3), 32.4 (t, 2 × C-2), 20.6 (q, 2 × *C*H$_3$CO), 17.5 (q, 2 × C-6); elemental analysis calcd (%) for $C_{24}H_{32}F_6N_2O_{10}$ (622.5): C 46.31, H 5.18, N 4.50; found C 46.00, H 5.63, N 4.37.

1,4-Di-(3′-trifluoroacetamido-2′,3′,6′-trideoxy-α-L-*ribo*-hexopyranosyl)-1,4-butanediol (23): PtO_2 (4 mg) was added to a solution of homodimer **25** (36 mg, 67 μmol) in ethyl acetate (6 mL). The suspension was stirred under H_2 atmosphere at room temperature for 16 h. The hydrogenation was terminated by addition of Et_3N (1 mL), followed by filtration and removal of the solvents in vacuo. The crude material obtained was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) to furnish the desired reduction product **23** as a colorless oil (26.2 mg, 49 μmol, 73%). $R_f = 0.11$ (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{21} = -34.3$ ($c = 1.31$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.13$ (d, $J = 7.8$ Hz, 2H; 2 × NH), 4.88 (d, $J = 2.4$ Hz, 2H; 2 × 1-H), 4.51 – 4.42 (m, 2H; 2 × 3-H), 3.81 – 3.74 (m, 2H; 2 × OC*H*H′), 3.71 (dq, $J = 9.8$, 6.0 Hz, 2H; 2 × 5-H), 3.54 (dd, $J = 9.6$, 3.8 Hz, 2H; 2 × 4-H), 3.48 – 3.40 (m, 2H; 2 × OCH*H*′), 2.09 (dt, $J = 14.8$, 3.8 Hz, 2H; 2 × 2-H_{eq}), 1.97 (ddd, $J = 14.8$, 3.0, 1.4 Hz, 2H; 2 × 2-H_{ax}), 1.70 (m, 4H; CH_2CH_2), 1.30 (d, $J = 6.0$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 159.5$ (q, 2 × CF_3CO), 116.0 (q, 2 × *C*F$_3$CO), 96.6 (d, 2 × C-1), 73.0 (d, 2 × C-4), 67.4 (t, 2 × OCH_2), 64.3 (d, 2 × C-5), 48.1 (d, 2 × C-3), 32.6 (t, 2 × C-2), 26.4 (t, 2 × *C*H$_2$CH$_2$O), 17.6 (q, 2 × C-6); elemental analysis calcd (%) for $C_{20}H_{30}F_6N_2O_8$ (540.5): C 44.45, H 5.59, N 5.18; found C 44.47, H 5.49, N 5.28.

Preparation of homodimer 23 via the 4′-*O*-acetyl protected dimer 30: PtO_2 (4 mg) was added to a solution of homodimer **28** containing traces of rearranged dimer **29** (48 mg, 77 μmol) in ethyl acetate (15 mL). The suspension was stirred under H_2 atmosphere at room temperature for 16 h.

  0947-6539/02/0812-2726 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

The hydrogenation was terminated by addition of Et_3N (1 mL), followed by filtration and removal of the solvents in vacuo. The crude material obtained was purified by flash column chromatography (petroleum ether/ethyl acetate 2:1) to furnish the desired reduction product **30** as a colorless oil (43 mg, 69 μmol, 89%). $R_f = 0.12$ (petroleum ether/ethyl acetate 2:1); $[\alpha]_D^{22} = -70.5$ ($c = 1.7$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.03$ (d, $J = 8.0$ Hz, 2H; 2 × NH), 4.90 (d, $J = 2.8$ Hz, 2H; 2 × 1-H), 4.64–4.59 (m, 2H; 2 × 3-H), 4.58 (dd, $J = 9.8$, 4.0 Hz, 2H; 2 × 4-H), 3.91 (dq, $J = 9.8$, 6.2 Hz, 2H; 2 × 5-H), 3.84–3.74 (m, 2H; 2 × OC*H*H′), 3.51–3.40 (m, 2H; 2 × OCH*H*′), 2.12 (dt, $J = 14.6$, 3.8 Hz, 2H; 2 × 2-H_{eq}), 1.99 (s, 6H; 2 × CH_3CO), 1.94 (ddd, $J = 14.6$, 2.6, 1.2 Hz, 2H; 2 × 2-H_{ax}), 1.71 (m, 4H; CH_2CH_2), 1.21 (d, $J = 6.0$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 170.2$ (s, 2 × CH_3*C*O), 156.8 (q, 2 × CF_3*C*O), 116.0 (q, 2 × *C*F_3CO), 96.8 (d, 2 × C-1), 72.3 (d, 2 × C-4), 67.6 (t, 2 × OCH_2), 61.8 (d, 2 × C-5), 44.7 (d, 2 × C-3), 32.5 (t, 2 × C-2), 26.5 (t, 2 × *C*H_2CH$_2$O), 20.6 (q, 2 × *C*H_3CO), 17.4 (q, 2 × C-6).

The compound obtained from above was dissolved in a mixture of 0.1M NaOH/THF (3:1) and stirred at room temperature for 0.5 h. The crude material obtained was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) to furnish the desired reduction product **23** (35 mg, 65 μmol, 94%).

Preparation of linear neotetrasaccharide 31: TMSOTf (10 μL, 54 μmol) was added under nitrogen to a suspension of head-to-head linked disaccharide **23** (36 mg, 67 μmol), silyl glycoside **14a** (62 mg, 0.16 mmol) in dry dichloromethane (16 mL), and powdered molecular sieves 3 Å. The reaction mixture was stirred for 1 d thereby raising the temperature from −60 to −40 °C after the first 0.5 h. After filtration and addition of aqueous bicarbonate solution to the organic layer, the filter cake was thoroughly washed with dichloromethane. The aqueous layer was washed with ethyl acetate (3 × 7 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude oil was purified by column chromatography (petroleum ether/ethyl acetate 3:2) to yield the target homodimer **31** (56 mg, 52 μmol, 78%). $R_f = 0.56$ (petroleum ether/ethyl acetate 2:3); $[\alpha]_D^{22} = -75.8$ ($c = 2.06$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.06$ (d, $J = 9.0$ Hz, 2H; 2 × NH), 6.32 (d, $J = 8.4$ Hz, 2H; 2 × NH′), 5.83 (ddt, $J = 17.2$, 10.2, 5.8 Hz, 2H; 2 × C*H*=), 5.24 (dq, $J = 17.2$, 1.4 Hz, 2H; 2 × C*H*′H=CH-), 5.23 (dd, $J = 3.8$, 1.1 Hz, 2H; 2 × 1-H′), 5.20 (dq, $J = 10.2$, 1.0 Hz, 2H; 2 × CH*H*′=CH), 4.89 (t, $J = 2.2$ Hz, 2H; 2 × 1-H), 4.58–4.53 (m, 2H; 2 × 3-H), 4.18–4.13 (m, 2H; 2 × 3-H′), 4.16 (ddt, $J = 12.3$, 6.5, 1.0 Hz, 2H; 2 × OC*H*′H), 3.95 (ddt, $J = 12.3$, 6.6, 1.0 Hz, 2H; OCH*H*′), 3.83–3.73 (m, 6H; 2 × 5-H, 2 × 5-H′and 2 × OC*H*H′), 3.50 (dd, $J = 9.7$, 3.6 Hz, 2H; 2 × 4-H), 3.47–3.43 (m, 2H; 2 × OCH*H*′), 3.01 (t, $J = 9.2$ Hz, 2H; 2 × 4-H′), 2.12 (dt, $J = 14.6$, 3.8 Hz, 2H; 2 × 2-H_{eq}), 1.94 (ddd, $J = 14.6$, 2.6, 1.2 Hz, 2H; 2 × 2-H_{ax}), 1.94 (ddd, $J = 13.0$, 4.8, 1.6 Hz, 2H; 2 × 2-H′$_{eq}$), 1.82 (dt, $J = 12.8$, 4.2 Hz, 2H; 2 × 2-H′$_{ax}$), 1.71 (m, 4H; CH_2CH_2), 1.30 (d, $J = 5.8$ Hz, 6H; 2 × 6-H′), 1.29 (d, $J = 6.2$ Hz, 6H; 2 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 156.8$ (q, 2 × *C*′OCF_3), 156.6 (q, 2 × *C*′OCF_3), 134.1 (d, 2 × =CH), 118.3 (t, 2 × CH_2=, 115.9, 115.8 (2q, 2 × *C*F_3CO and 2 × *C*′F_3CO), 96.7 (d, 2 × C-1), 92.2 (d, 2 × C-1′), 82.0 (d, 2 × C-4′), 73.4 (t, 2 × OC′H_2), 73.3 (d, 2 × C-4), 68.4 (d, 2 × C-5′), 67.4 (t, 2 × OCH_2), 62.8 (d, 2 × C-5), 48.5 (d, 2 × C-3′), 43.0 (d, 2 × C-3), 34.6, 34.5 (2t, 2 × C-2′), 32.6 (t, 2 × C-2), 26.5 (t, 2 × *C*H_2CH$_2$O), 18.6 (q, 2 × C-6′), 18.1 (q, 2 × C-6); LRMS (ES) (−c): *m*/*z* (%): 1069.9 (100) $[M-H]^-$, 1071 (55) $[M]^-$; (+c): 1093.5 (100) $[M+Na]^+$.

Preparation of macrocyclic disaccharide 32 by ring-closing metathesis: Diene **15** (30 mg, 48 μmol) was dried under reduced pressure (10^{-2} Torr) for 2.5 h and was dissolved under nitrogen in absolute benzene (40 mL). To this solution was added catalyst **8** (10 mg, 13 mol%) and the purple solution was stirred at 47 °C for 24 h, at which time the reaction was terminated by concentration under reduced pressure. After addition of diethyl ether (20 mL) and triethylamine (1 mL) stirring was continued under air for 2 h. The solvents were removed under reduced pressure to afford an oil, which was purified by column chromatography (silica gel; petroleum ether/ethyl acetate 4:1) to yield macrocyclic disaccharide **32** as colorless crystals (19.1 mg, 32 μmol; 67%) as well as recovered starting material **15** (6 mg, 9.7 μmol, 20%). Compound **32**: m.p. 218–220 °C; $[\alpha]_D^{22} = -111.2$ ($c = 0.96$ in $CHCl_3$/MeOH 5:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.97$ (d, $J = 9.0$ Hz, 2H; 2 × NH), 5.82 (t, $J = 3.2$ Hz, 2H; 2 × CH=), 4.78 (d, $J = 2.4$ Hz, 2H; 2 × 1-H), 4.54–4.37 (m, 2H; 2 × 3-H), 4.06 (ddd, $J = 12.0$, 3.0, 1.5 Hz, 2H; 2 × OC*H*H′), 3.96 (ddd, $J = 12.0$, 3.0, 1.5 Hz, 2H; 2 × OCH*H*′), 3.87 (dq, $J = 9.6$, 6.0 Hz, 2H; 2 × 5-H), 3.55–3.38 (m, 4H; 2 × OCH_2), 2.93 (t, $J = 9.8$ Hz, 2H; 2 × 4-H), 2.05 (ddd, $J = 12.8$, 4.8, 1.1 Hz, 2H; 2 × 2-H_{eq}), 1.65 (dt, $J = 12.6$, 3.4 Hz, 2H; 2 × 2-H_{ax}), 1.47 (m, 4H; 2 × OCH_2CH_2), 1.30 (d, $J = 6.3$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 157.2$ (q, 2 × *C*OCF_3), 129.0 (d, 2 × CH=), 115.9 (q, 2 × CO*C*F_3), 96.0 (d, 2 × C-1), 81.0 (d, 2 × C-4), 68.5 (t, 2 × OCH_2), 66.7 (t, 2 × OCH_2), 66.3 (d, 2 × C-5), 45.7 (d, 2 × C-3), 35.4 (t, 2 × C-2), 28.0 (t, 2 × *C*H_2CH$_2$O), 18.0 (q, 2 × C-6). The material was directly used for the next step.

Preparation of macrocyclic disaccharide 3: Macrocyclic disaccharide **32** (19 mg, 32 μmol) was stirred in a mixture of THF/0.1M aqueous NaOH (1:3, 12 mL) at room temperature for 5 h. After addition of dry ice (pH 7–8) the solution was concentrated to 0.5 mL under reduced pressure and the resulting material was subjected to a small column (reversed phase; C-18; gradient $H_2O \rightarrow$ MeOH) to yield the target neosaccharide **3** (single *E* isomer: 12 mg, 30 μmol, 94%). $[\alpha]_D^{23} = -25.9$ ($c = 0.61$ in $CHCl_3$/MeOH 3:1); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.84$ (t, $J = 2.6$ Hz, 2H; 2 × CH=), 4.84 (d, $J = 2.5$ Hz, 2H; 2 × 1-H), 4.15 (ddd, $J = 12.0$, 3.0, 1.5 Hz, 2H; 2 × OC*H*H′), 4.02 (ddd, $J = 12.0$, 3.0, 1.5 Hz, 2H; 2 × OC*H*H′), 3.84 (dq, $J = 9.7$, 6.3 Hz, 2H; 2 × 5-H), 3.73–3.65 (m, 2H; 2 × OCH*H*′), 3.62–3.55 (m, 2H; 2 × OC*H*H′), 3.34 (ddd, $J = 12.0$, 9.8, 4.6 Hz, 2H; 2 × 3-H), 2.74 (t, $J = 9.6$ Hz, 2H; 2 × 4-H), 2.04 (ddd, $J = 13.2$, 4.8, 1.0 Hz, 2H; 2 × 2-H_{eq}), 1.73–1.69 (m, 4H; 2 × OCH_2CH_2), 1.55 (br s, 4H; 2 × NH_2), 1.53 (dt, $J = 12.4$, 3.4 Hz, 2H; 2 × 2-H_{ax}), 1.29 (d, $J = 6.1$ Hz, 6H; 2 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 128.6$ (d, 2 × CH=), 97.2 (d, 2 × C-1), 86.0 (d, 2 × C-4), 68.7 (t, 2 × OCH_2), 68.0 (t, 2 × OCH_2), 66.1 (d, 2 × C-5), 46.4 (d, 2 × C-3), 38.4 (t, 2 × C-2), 28.4 (t, 2 × *C*H_2CH$_2$O), 18.5 (q, 2 × C-6); DCI-MS: *m*/*z* (%): 401.5 (100) $[M+H]^+$, 801.9 (3) $[2M+H]^+$.

Preparation of macrocyclic tetrasaccharide 33: A suspension of macrocyclic alkene **32** (16 mg, 27 μmol) and PtO_2 (4 mg) in dichloromethane/methanol (10:1, 10 mL) was stirred under an H_2 atmosphere at room temperature for 16 h. After removal of the catalyst by filtration the mixture was concentrated under reduced pressure to afford a crude product which was purified by flash column chromatography (petroleum ether/ethyl acetate 2:1). The title compound was obtained as colorless crystals (14 mg, 24 μmol, 87%). M.p. 118–220 °C; $[\alpha]_D^{22} = -62.5$ ($c = 0.78$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 6.20$ (d, $J = 7.4$ Hz, 2H; 2 × NH), 4.81 (dd, $J = 3.0$, 1.2 Hz, 2H; 2 × 1-H), 4.54–4.38 (m, 2H; 2 × 3-H), 3.96 (dq, $J = 9.2$, 6.2 Hz, 2H; 2 × 5-H), 3.71 (dt, $J = 9.2$, 6.2 Hz, 2H; 2 × OC*H*H′), 3.59–3.49 (m, 4H; 2 × OCH_2), 3.49 (dt, $J = 9.2$, 6.2 Hz, 2H; 2 × OCHOC*H*H′), 3.01 (t, $J = 9.6$ Hz, 2H; 2 × 4-H), 2.26 (ddd, $J = 12.8$, 4.8, 1.5 Hz, 2H; 2 × 2-H_{eq}), 1.69 (dt, $J = 12.4$, 3.5 Hz, 2H; 2 × 2-H_{ax}), 1.69–1.53 (m, 8H; 2 × OCHOCH_2CH_2 and 2 × OCH_2CH_2), 1.35 (d, $J = 6.3$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 157.1$ (q, 2 × *C*OCF_3), 115.9 (q, 2 × CO*C*F_3), 95.9 (d, 2 × C-1), 81.4 (d, 2 × C-4), 68.7 (t, 2 × C4-OCH_2), 67.2 (t, 2 × OCHO*C*H_2), 66.0 (d, 2 × C-5), 46.6 (d, 2 × C-3), 35.7 (t, 2 × C-2), 27.9 (t, 2 × *C*H_2CH$_2$O), 27.3 (t, 2 × CH_2CH_2O), 18.5 (q, 2 × C-6); LRMS (ES) (+c): m/z (%): 617.6 (100) $[M+Na]^+$, 1211.3 (60) $[2M+Na]^+$; (−c) 594.6 (54) $[M]^-$, 593.7 (72) $[M-H]^-$.

Preparation of macrocyclic disaccharide 4: Macrocyclic disaccharide **33** (26 mg, 44 μmol) was stirred in a mixture of THF/0.1M aqueous NaOH (1:3, 12 mL) at room temperature for 5 h. After addition of dry ice (pH 7–8) the solution was concentrated (to 0.5 mL) under reduced pressure and the resulting material was subjected to a small column (reversed phase; C-18; gradient $H_2O \rightarrow$ MeOH) to yield the target neosaccharide **4** as a semisolid (15 mg, 37 μmol; 85%). $[\alpha]_D^{23} = -57$ ($c = 0.51$ in $CHCl_3$/MeOH 3:1); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 4.73$ (d, $J = 2.8$ Hz, 2H; 2 × 1-H), 3.81 (dq, $J = 9.2$, 6.2 Hz, 2H; 2 × 5-H), 3.73–3.66 (m, 2H; 2 × OC*H*H′), 3.68 (dt, $J = 9.1$, 6.0 Hz, 2H; 2 × OCHOC*H*H′), 3.61–3.55 (m, 2H; 2 × OCH*H*′), 3.38 (dt, $J = 9.1$, 6.0 Hz, 2H; 2 × OCHOCH*H*′), 3.28 (ddd, $J = 12.0$, 9.8, 4.6 Hz, 2H; 2 × 3-H), 2.72 (t, $J = 9.6$ Hz, 2H; 2 × 4-H), 2.22 (br s, 4H; 2 × NH_2), 1.96 (ddd, $J = 13.0$, 4.6, 0.8 Hz, 2H; 2 × 2-H_{eq}), 1.75–1.70 (m, 2H; 2 × OCHOCH_2C*H*H′), 1.69 (m, 4H; CH_2CH_2), 1.53–1.48 (m, 2H; 2 × OCHOCH_2CH*H*′), 1.49 (dt, $J = 12.4$, 3.4 Hz, 2H; 2 × 2-H_{ax}), 1.26 (d, $J = 6.2$ Hz, 6H; 2 × 6-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 96.7$ (d, 2 × C-1), 85.6 (d, 2 × C-4), 68.7 (t, 2 × OCH_2), 67.9 (t, 2 × OCHOCH_2), 65.6 (d, 2 × C-5), 46.0 (d, 2 × C-3), 38.0 (t, 2 × C-2), 27.9 (t, 2 × *C*H_2CH$_2$O), 27.2 (t, 2 × *C*H_2CH$_2$OCHO), 18.6 (q, 2 × C-6); DCI-MS: *m*/*z* (%): 403.4 (100) $[M+H]^+$.

Preparation of macrocyclic tetrasaccharide 34 and macrocyclic hexasaccharide 35 by ring-closing metathesis and catalytic hydrogenation: Diene **19** (32 mg, 52 μmol) was dried under reduced pressure (10^{-2} Torr) for 2.5 h and then was dissolved under nitrogen in absolute benzene (40 mL). To this solution was added catalyst **8** (8.5 mg, 9.9 mol%) and the purple solution was stirred at 50 °C for 14 h, at which time the reaction was terminated by concentration under reduced pressure. After addition of diethyl ether (20 mL) and triethylamine (1 mL) stirring was continued under air for 2 h. The solvents were removed under reduced pressure to afford an oil, which was purified by column chromatography (petroleum ether/ethyl acetate 2:1) to yield macrocyclic tetrasaccharide (20 mg, 17 μmol, 64%; two isomers 3:1) and hexasaccharide (5 mg, 2.8 μmol, 16.2%; two isomers 3:1).

1st Fraction: Tetrasaccharide; $R_f = 0.30$ (petroleum ether/ethyl acetate 1:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.80$ (d, $J = 9.2$ Hz, 4H; 4 × NH), 5.82 (m, 4H; 4 × CH=), 4.90 (t, $J = 2.0$ Hz, 4H; 4 × 1-H), 4.62 (m, 4H; 4 × 3-H), 4.22 (m, 4H; 4 × OCHOC*H*H′), 3.94 (m, 4H; 4 × OCHOCH*H*′), 3.84–3.70 (m, 4H; 4 × OC*H*H′), 3.70 (dq, $J = 9.8$, 6.2 Hz, 4H; 4 × 5-H), 3.35–3.22 (m, 4H; 4 × OCH*H*′), 3.04 (dd, $J = 9.8$, 3.8 Hz, 4H; 4 × 4-H), 1.99–1.96 (m, 8H; 4 × 2-H_{eq}, 4 × 2-H_{ax}), 1.52 (m, 8H; 2 × CH_2CH_2), 1.27 (d, $J = 6.4$ Hz, 12H; 4 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta =$ 156.8 (q, 4 × *C*OCF_3), 128.9 (d, 4 × =CH), 116.0 (q, 4 × CO*C*F_3), 95.8 (d, 4 × C-1), 78.8 (d, 4 × C-4), 69.6 (t, 4 × OCH_2), 67.1 (t, 4 × OCHO*C*H_2), 63.5 (d, 4 × C-5), 43.6 (d, 4 × C-3), 32.8 (t, 4 × C-2), 26.4 (t, 4 × *C*H_2CH_2O), 17.9 (q, 4 × C-6); LRMS (ES) (−c): *m*/*z* (%): 1184.2 (100) $[M]^-$; (+c): 1207.8 (100) $[M+Na]^+$; selected NMR data for minor isomer: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.77$ (m, 4H, 4 × CH=); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 61.4$ (t, 4 × OCHO*C*H_2).

2nd Fraction: Hexasaccharide; $R_f = 0.20$ (petroleum ether/ethyl acetate 1:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.82$ (d, $J = 8.4$ Hz, 6H; 6 × NH), 5.82 (m, 6H; 6 × CH=), 4.89 (t, $J = 2.0$ Hz, 6H; 6 × 1-H), 4.62 (m, 6H; 6 × 3-H), 4.27–4.15 (m, 6H; 6 × OCHOC*H*H′), 4.02–3.91 (m, 6H; 6 × OCHOCH*H*′), 3.84–3.70 (m, 6H; 6 × OC*H*H′), 3.70 (dq, $J = 9.8$, 6.2 Hz, 6H; 6 × 5-H), 3.35–3.22 (m, 6H; 6 × OCH*H*′), 3.05 (dd, $J = 9.8$, 3.8 Hz, 6H; 6 × 4-H), 1.99 (m, 12H; 6 × 2-H_{eq} and 6 × 2-H_{ax}), 1.52 (m, 12H; 3 × CH_2CH_2), 1.27 (d, $J = 6.0$ Hz, 18H; 6 × 6-H); LRMS (ES) (−c): *m*/*z* (%): 1776.3 (100) $[M]^-$; (+c): 1799.8 (100) $[M+Na]^+$.

A suspension of the macrocyclic tetrasaccharide described above (20 mg, 17 μmol) and PtO_2 (4 mg) in ethyl acetate (8 mL) was stirred under an hydrogen atmosphere at room temperature for 16 h. After removal of the catalyst by filtration the mixture was concentrated under reduced pressure to afford a crude product which was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) to yield macrocyclic tetramer **34** as colorless crystals (20 mg, 17 μmol, 99%). $R_f = 0.36$ (petroleum ether/ethyl acetate 2:3); m.p. 133–135 °C; $[\alpha]_D^{22} = -98.6$ ($c = 0.77$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.80$ (d, $J = 9.2$ Hz, 4H; 4 × NH), 4.85 (t, $J = 2.0$ Hz, 4H; 4 × 1-H), 4.59 (m, 4H; 4 × 3-H), 3.84–3.70 (m, 4H; 4 × OCHOC*H*H′), 3.82–3.62 (m, 4H; 4 × OCHOCH*H*′), 3.70 (dq, $J =$ 9.8, 6.2 Hz, 4H; 4 × 5-H), 3.44–3.34 (m, 4H; 4 × OCHOCH*H*′), 3.32–3.22 (m, 4H; 4 × OC*H*H′), 3.02 (dd, $J = 9.4$, 4.0 Hz, 4H; 4 × 4-H), 1.97 (m, 8H; 4 × 2-H_{eq}, 4 × 2-H_{ax}), 1.74–1.64 (m, 8H; 4 × CH_2CH_2), 1.52 (m, 8H; 4 × CH_2CH_2), 1.27 (d, $J = 6.4$ Hz, 12H; 4 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 156.8$ (q, 4 × *C*OCF_3), 116.0 (q, 4 × CO*C*F_3), 96.6 (d, 4 × C-1), 78.7 (d, 4 × C-4), 69.8 (t, 4 × OCH_2), 67.2 (t, 4 × OCHO*C*H_2), 63.4 (d, 4 × C-5), 43.7 (d, 4 × C-3), 32.7 (t, 4 × C-2), 26.8 (t, 8 × *C*H_2CH_2O), 17.8 (q, 4 × C-6); LRMS (ES) (+c): *m*/*z* (%): 1211.7 (100) $[M+Na]^+$.

Accordingly, a suspension of the macrocyclic hexasaccharide described above (12 mg, 6.8 μmol) and PtO_2 (3 mg) in ethyl acetate (8 mL) was stirred under an hydrogen atmosphere at room temperature for 16 h. After removal of the catalyst by filtration the mixture was concentrated under reduced pressure to afford a crude product which was purified by flash column chromatography (petroleum ether/ethyl acetate 1:2) to yield macrocyclic hexamer **35** (12 mg, 6.7 μmol, 99%). $R_f = 0.16$ (petroleum ether/ethyl acetate 2:3); $[\alpha]_D^{22} = -86.4$ ($c = 0.28$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.83$ (d, $J = 9.2$ Hz, 6H; 6 × NH), 4.85 (t, $J = 2.0$ Hz, 6H; 6 × 1-H), 4.60 (m, 6H; 6 × 3-H), 3.82–3.73 (m, 12H; 12 × OC*H*H′), 3.70 (dq, $J = 9.6$, 6.2 Hz, 6H; 6 × 5-H), 3.41, 3.29 (m, 12H; 12 × OCH*H*′), 3.04 (dd, $J = 9.6$, 3.8 Hz, 6H; 6 × 4-H), 1.98 (m, 12H; 6 × 2-H_{eq}, 6 × 2-H_{ax}), 1.68, 1.52 (m, 24H; 6 × *C*H_2CH_2), 1.27 (d, $J = 6.2$ Hz, 18H; 6 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 156.8$ (q, 6 × *C*OCF_3), 116.0 (q, 6 × CO*C*F_3), 96.7 (d, 6 × C-1), 78.8 (d, 6 × C-4), 69.5 (t, 6 × O*C*H_2), 67.4 (t, 6 × OCHO*C*H_2), 63.4 (d, 6 × C-5), 43.6 (d, 6 × C-3), 32.8 (t, 6 × C-2), 26.4 (t, 12 × *C*H_2CH_2O), 17.9 (q, 6 × C-6); LRMS (ES) (+c): *m*/*z* (%): 1806.0 (100) $[M+Na]^+$.

Preparation of macrocyclic tetrasaccharide 5: Macrocyclic disaccharide **34** (20 mg, 17 μmol) was stirred in a mixture of THF/1.0 M aqueous NaOH (1:2, 12 mL) at 50 °C for 30 h. After addition of dry ice (pH 7–8) the solution was concentrated (to 0.5 mL) under reduced pressure and the resulting material was subjected to a small column (reversed phase; C-18; gradient $H_2O \rightarrow$ MeOH) to yield the target neosaccharide **5** as a light green semisolid (14 mg, 17 μmol, 99%). $[\alpha]_D^{22} = -127.9$ ($c = 0.77$ in $CHCl_3$/MeOH 3:1); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 4.75$ (d, $J = 3.6$ Hz, 4H; 4 × 1-H), 3.81 (dq, $J = 9.6$, 6.0 Hz, 4H; 4 × 5-H), 3.70–3.64 (m, 4H; 4 × OCHOC*H*H′), 3.64–3.58 (m, 4H; 4 × OC*H*H′), 3.38–3.32 (m, 4H; 4 × OCH*H*′), 3.32–3.27 (m, 4H; 4 × OCHOCH*H*′), 3.26 (m, 4H; 4 × 3-H), 3.29 (dd, $J = 9.8$, 3.8 Hz, 4H; 4 × 4-H), 2.03 (dd, $J = 14.4$, 2.4 Hz, 4H; 4 × 2-H_{eq}), 1.99 (br s, 8H; 4 × NH_2), 1.84 (dt, $J = 14.4$, 4.4 Hz, 4H; 4 × 2-H_{ax}), 1.68–1.61 (m, 16H; 4 × CH_2CH_2), 1.26 (d, $J = 6.2$ Hz, 12H; 4 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 97.3$ (d, 4 × C-1), 81.7 (d, 4 × C-4), 69.0 (t, 4 × OCH_2), 67.5 (t, 4 × OCHO*C*H_2), 61.5 (d, 4 × C-5), 45.3 (d, 4 × C-3), 34.1 (t, 4 × C-2), 27.1 and 26.9 (t, 8 × *C*H_2CH_2O), 18.0 (q, 4 × C-6); DCI-MS: *m*/*z* (%): 805.8 (100) $[M+H]^+$.

Preparation of macrocyclic tetrasaccharide 36 from diene 31: Diene **31** (56 mg, 52 μmol) was dried under reduced pressure (10^{-2} Torr) for 2.5 h and was dissolved under nitrogen in absolute benzene (30 mL). To this solution was added catalyst **8** (9 mg, 20 mmol%) and the purple solution was stirred at 50 °C for 24 h, at which time the reaction was terminated by concentration under reduced pressure. After addition of diethyl ether (20 mL) and triethylamine (1 mL) stirring was continued under air for 2 h. The solvents were removed in vacuo to afford an oil, which was dissolved in ethyl acetate (10 mL). After addition of PtO_2 (4 mg), the suspension was stirred under H_2 at rt for 16 h. After removal of the catalyst by filtration the mixture was evaporated under reduced pressure to afford a crude product which was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) yielding tetrasaccharide **36** (12 mg, 12 μmol, 22.1%). $R_f = 0.59$ (petroleum ether/ethyl acetate 2:3); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.02$ (d, $J = 8.8$ Hz, 2H; 2 × NH), 6.09 (d, $J = 8.3$ Hz, 2H; 2 × NH′), 5.25 (d, $J = 3.1$ Hz, 2H; 2 × 1-H′), 4.89 (s, 2H; 2 × 1-H), 4.61–4.55 (m, 2H; 2 × 3-H), 4.32–4.22 (m, 2H; 2 × 3-H′), 3.95 (dq, $J = 9.6$, 6.3 Hz, 2H; 2 × 5-H′), 3.82 (dq, $J = 9.6$, 6.0 Hz, 2H; 2 × 5-H), 3.84–3.78 (m, 2H; 2 × OC*H*H′), 3.71–3.66 (m, 4H; 2 × OCH_2 at C4′), 3.56 (dd, $J = 10.0$, 3.8 Hz, 2H; 2 × 4-H), 3.37 (m, 2H; 2 × OCH*H*′), 2.92 (t, $J = 9.8$ Hz, 2H; 2 × 4-H′), 2.06–2.00 (m, 4H; 2 × 2-H_{eq}, 2 × 2-H_{ax}), 1.90–1.70 (m, 10H; 2 × 2-H'_{eq}, *C*H_2CH_2, *C*$H'_2CH'_2$), 1.66 (ddd, $J = 13.2$, 12.0, 3.8 Hz, 2H; 2 × 2-H'_{ax}), 1.42 (d, $J = 6.0$ Hz, 6H; 2 × 6-H′), 1.25 (d, $J = 6.0$ Hz, 6H; 2 × 6-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 156.8$ (q, 2 × *C*OCF_3), 156.6 (q, 2 × *C*′OCF_3), 116.0, 115.8 (2q, 2 × *C*F_3CO, 2 × *C*′F_3C′O), 97.7 (d, 2 × C-1), 92.1 (d, 2 × C-1′), 81.5 (d, C-4′), 73.1 (d, 2 × C-4), 69.1, 68.9 (2t, 4 × O*C*H_2), 67.0 (d, 2 × C-5′), 63.2 (d, 2 × C-5), 46.1 (d, 2 × C-3′), 43.0 (d, 2 × C-3), 35.7 (t, 2 × C-2′), 32.7 (t, 2 × C-2), 28.0, 27.0 (t, 4 × *C*H_2CH_2O), 18.5 (q, 2 × C-6′), 18.0 (q, 2 × C-6); DCI-MS: *m*/*z* (%): 1062.8 (100) $[M+NH_4]^+$.

Preparation of cyclic neotetrasaccharide 7: Macrocyclic tetrasaccharide **36** (12 mg, 11.5 μmol) was stirred in a mixture of THF/0.4 M aqueous NaOH (1:3, 8 mL) at room temperature for 18 h. After addition of dry ice (pH 7–8) the solution was concentrated (to 0.5 mL) under reduced pressure and the resulting material was subjected to a small column (reversed phase; C-18; gradient $H_2O \rightarrow$ MeOH) to yield the target neosaccharide **7** (6 mg, 9 μmol, 78%). $[\alpha]_D^{22} = -99.5$ ($c = 0.195$ in $CHCl_3$/MeOH 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 4.93$ (d, $J = 3.2$ Hz, 2H; 2 × 1-H′), 4.77 (d, $J = 3.6$ Hz, 2H; 2 × 1-H), 3.93 (dq, $J = 9.6$, 6.2 Hz, 2H; 2 × 5-H), 3.85 (dq, $J = 9.2$, 6.0 Hz, 2H; 2 × 5-H′), 3.71–3.55 (m, 6H; 3 × OCH_2), 3.48 (m, 2H; 2 × OCH_2), 3.37 (dd, $J = 9.6$, 3.4 Hz, 2H; 2 × 4-H), 3.27–3.22 (m, 4H; 2 × 3-H and 2 × 3-H′), 2.72 (t, $J = 9.6$ Hz, 2H; 2 × 4-H′), 2.04 (ddd, $J = 14.0$, 2.8, 1.0 Hz, 2H; 2 × H_{eq}), 1.95 (ddd, $J = 13.0$, 4.6, 1.2 Hz, 2H; 2 × 2-H′$_{eq}$), 1.86 (dt, $J = 14.0$, 4.4 Hz, 2H; 2 × 2-H_{ax}), 1.76–1.67 (m, 8H; 2 × CH_2CH_2), 1.59 (dt, $J = 12.2$, 3.4 Hz, 2H; 2 × 2-H′$_{ax}$), 1.32 (d, $J = 6.2$ Hz, 2H; 2 × 6-H′), 1.26 (d, $J = 6.4$ Hz, 6H; 2 × 6-H); ^{13}C NMR (100 MHz, HMQC, $CDCl_3$, 25 °C, TMS): $\delta = 97.8$ (d, 2 × C-1), 92.3 (d, 2 × C-1′), 86.0 (d, C-4′), 76.6 (d, 2 × C-4), 70.0, 69.6 (2t, 4 × OCH_2), 67.2 (d, 2 × C-5′), 61.7 (d, 2 × C-5), 46.9 (d, 2 × C-3′), 44.4 (d, 2 × C-3), 39.1 (t, 2 × C-2′), 34.7 (t, 2 × C-2), 28.4 (t, 4 × *C*H_2CH_2O); DCI-MS: *m*/*z* (%): 661.7 (14) $[M+H]^+$.

0947-6539/02/0812-2728 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 12

Acknowledgement

This work was supported by the Deutsche Forschungsgemeinschaft (SFB 416) and the Fonds der Chemischen Industrie. This project is part of the joint initiative "Biologisch Aktive Naturstoffe—Synthetische Diversität" at the Universität Hannover.

[1] a) C. Bailly, J.-P. Hénichart, in *Molecular Aspects of Anticancer Drug-DNA Interactions*, *Vol. 2* (Eds.: S. Neidle, M. Waring), Macmillan Press, London, **1994**, p. 162–196; b) K. C. Nicolaou, A. L. Smith, in *Modern Acetylene Chemistry* (Eds.: P. J. Stang, F. Diederich), VCH, Weinheim, **1995**.

[2] Reviews: a) W. D. Wilson, K. Li, *Curr. Med. Chem.* **2000**, *7*, 73–98; b) D. E. Graves, L. M. Velea, *Curr. Org. Chem.* **2000**, *4*, 915–929.

[3] K. Michael, Y. Tor, *Chem. Eur. J.* **1998**, *4*, 2091–2098.

[4] a) U. von Ahsen, J. Davies, R. Schroeder, *J. Mol. Biol.* **1992**, *226*, 935–941; b) J. Davies, U. von Ahsen, R. Schroeder, *The RNA World*, Cold Spring Harbor Laboratory Press, New York, **1993**, p. 185–204; c) U. von Ahsen, J. Davies, R. Schroeder, *Nature* **1991**, *353*, 368–370; d) U. von Ahsen, H. F. Noller, *Science* **1993**, *260*, 1500–1503; e) M. L. Zapp, S. Stern, M. R. Green, *Cell* **1993**, *74*, 969–978; f) M. L. Zapp, D. W. Young, A. Kumar, R. Singh, D. W. Boykin, W. D. Wilson, M. R. Green, *Bioorg. Med. Chem.* **1997**, *5*, 1149–1155; g) M. Hendrix, E. S. Priestly, G. F. Joyce, C. Wong, *J. Am. Chem. Soc.* **1997**, *119*, 3641–3648; h) N. W. Luedtke, T. J. Baker, M. Goodman, Y. Tor, *J. Am. Chem. Soc.* **2000**, *122*, 12035–12036.

[5] a) H.-Y. Mei, A. A. Galan, N. S. Halim, D. P. Mack, D. W. Moreland, K. B. Sanders, H. N. Truong, A. W. Czarnik, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2755–2760; b) S. Wang, P. W. Huber, M. Cui, A. W. Czarnik, H.-Y. Mei, *Biochemistry* **1998**, *37*, 5549–5557; c) F. Hamy, V. Brondani, A. Flörsheimer, W. Stark, M. J. J. Blommers, T. Klimkait, *Biochemistry* **1998**, *37*, 5086–5095; d) H. Y. Mei, M. Cui, A. Heldsinger, S. M. Lemrow, J. A. Loo, K. A. Sannes-lowry, L. Sharmeen, A. W. Czarnik, *Biochemistry* **1998**, *37*, 14204–14212; e) N. W. Luedtke, T. J. Baker, M. Goodman, Y. Tor, *J. Am. Chem. Soc.* **2000**, *122*, 12035–12036.

[6] a) D. Fourmy, M. I. Recht, S. C. Blanchard, J. D. Puglisi, *Science* **1996**, *274*, 1269–1432; b) D. Fourmy, M. I. Recht, J. D. Puglisi, *J. Mol. Biol.* **1998**, *277*, 347–362; c) D. Fourmy, S. Yoshizawa, J. D. Puglisi, *J. Mol. Biol.* **1998**, *277*, 333–345; d) M. I. Recht, D. Fourmy, S. C. Blanchard, K. D. Dahlquist, J. D. Puglisi, *J. Mol. Biol.* **1996**, *262*, 421–436.

[7] a) T. K. Stage, K. J. Hertel, O. C. Uhlenbeck, *RNA* **1995**, *1*, 95–101; b) H. Wang, Y. Tor, *J. Am. Chem. Soc.* **1997**, *119*, 8734–8735; c) B. Clouet-d'Orval, T. K. Stage, O. C. Uhlenbeck, *Biochemistry* **1995**, *34*, 11186–11190; d) T. Hermann, E. Westhof, *J. Mol. Biol.* **1998**, 276, 903–912; e) H. Wang, Y. Tor, *Angew. Chem.* **1998**, *109*, 117–120; *Angew. Chem. Int. Ed.* **1998**, *37*, 109–111; f) D. J. Earnshaw, M. J. Gait, *Nucleic Acids Res.* **1998**, *26*, 5551–5561.

[8] a) R. Schroeder, C. Waldsich, H. Wank, *EMBO* **2000**, *19*, 1–9; b) S. R. Lynch, J. D. Puglisi, *J. Mol. Biol.* **2001**, *306*, 1037–1058; c) L. Varani, M. G. Spillantini, M. Goedert, G. Varani, *Nucl. Acids Res.* **2000**, *28*, 710–719; d) J. Cho, R. R. Rando, *Biochemistry* **1999**, *38*, 8548–8554; e) C. Faber, H. Sticht, K. Schweimer, P. Rösch, *J. Biol. Chem.* **2000**, *275*, 20660–20666.

[9] a) A. Kirschning, G.-w. Chen, *Synthesis* **2000**, 1133–1137; b) A. Kirschning, G.-w. Chen, *Tetrahedron Lett.* **1999**, *40*, 4665–4668.

[10] For related syntheses to linear neooligosaccharides refer to a) R. Roy, S. K. Das, *Chem. Commun.* **2000**, 519–529; b) R. Dominique, S. K. Das, R. Roy, *Chem. Commun.* **1998**, 2437–2438; c) R. Roy, R. Dominique, S. K. Das, *J. Org. Chem.* **1999**, *64*, 5408–5412; d) P. Hadwiger, A. E. Stütz, *Synlett* **1999**, 1787–1789.

[11] An excellent review, describing the factors which are important for cooperative effects in biological systems has been published by: M. Mammen, S.-K. Choi, G. M. Whitesides, *Angew. Chem.* **1998**, *110*, 2908–2953; *Angew. Chem. Int. Ed.* **1998**, *37*, 2754–2794.

[12] a) *Alkene Metathesis in Organic Synthesis* (Ed.: A. Fürstner), Springer Verlag, Berlin, Heidelberg, **1999**; b) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413–4450; c) K. J. Ivin, *J. Mol. Catal. A Chem.* **1998**, *133*, 1–16; d) M. Randall, M. L. Snapper, *J. Mol. Catal. A Chem.* **1998**, *133*, 29–40; e) S. K. Armstrong, *J. Chem. Soc. Perkin Trans. 1* **1998**, 371–388; f) M. Schuster, S. Blechert, *Angew. Chem.* **1997**, *108*, 2124–2144; *Angew. Chem. Int. Ed.* **1997**, *36*, 2036–2055; g) R. H. Grubbs, S. J. Miller, G. C. Fu, *Acc. Chem. Res.* **1995**, *28*, 446–452.

[13] a) M. Chmielewski, J. Jurczak, A. Zamojski, *Tetrahedron* **1978**, *34*, 2977–2981; b) J.-C. Florent, C. Monneret, *J. Chem. Soc. Chem. Commun.* **1987**, 1171–1172.

[14] a) L. F. Tietze, R. Fischer, H. J. Guder, A. Goerlach, M. Neumann, T. Krach, *Carbohydr. Res.* **1987**, *164*, 177–194; b) L. F. Tietze, R. Fischer, M. Loegers, M. Beller, *Carbohydr. Res.* **1989**, *194*, 155–162; c) Y. Kimura, M. Suzuki, T. Matsumoto, R. Abe, S. Terashima, *Chem. Lett.* **1984**, 501–504.

[15] C. Kolar, K. Dehmel, H. Moldenhauer, M. Gerken, *J. Carbohydr. Chem.* **1990**, *9*, 873–890.

[16] Guang-wu Chen, Ph.D. thesis, Technical University of Clausthal (Germany), **2001**.

[17] Y. St.-Denis, J.-F. Lavallee, D. Nguyen, G. Attardo, *Synlett* **1995**, 272–274.

[18] Assignment of the *trans* and *cis* stereoisomers was based on chemical shifts in the ^{13}C NMR spectra: a) E. Breitmaier, W. Voelter, in *Carbon-13 NMR Spectroscopy High Resolution Methods and Applications in Organic Chemistry and Biochemistry*, VCH, New York, **1987**, pp. 192; b) S. T. Diver, S. L. Schreiber, *J. Am. Chem. Soc.* **1997**, *119*, 5106–5109.

[19] A. Marra, J. Esnault, A. Veyrières, P. Sinaÿ, *J. Am. Chem. Soc.* **1992**, *114*, 6354–6360.

[20] P. A. Gent, R. Gigg, *J. Chem. Soc. Chem. Commun.* **1974**, 277.

[21] E. J. Corey, J. William Suggs, *J. Org. Chem.* **1973**, *38*, 3224–3224.

[22] Traces of the α,β- and β,β diastereoisomers were not isolated.

[23] a) R. T. Lee, Y. C. Lee, *Carbohydr. Res.* **1974**, *37*, 193–201; b) H. A. El-Shenawy, C. Schuerch, *Carbohydr. Res.* **1984**, *131*, 227–238.

[24] a) A. Nasreen, *Synlett* **2001**, 1341–1342; b) S. Hoyer, P. Laszlo, M. Horlovic, E. Polla, *Synthesis* **1986**, 655–657.

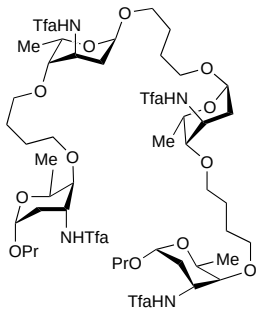
[25] B. Abbaci, J.-C. Florent, C. Monneret, *Bull. Soc. Chim. Fr.* **1989**, *5*, 667–672.

[26] S. T. Diver, S. L. Schreiber, *J. Am. Chem. Soc.* **1997**, *119*, 5106–5109.

[27] a) A. Fürstner, T. Müller, *J. Org. Chem.* **1998**, *63*, 424–425; b) A. Fürstner, M. Picquet, C. Bruneau, P. H. Dixneuf, *J. Chem. Soc. Chem. Commun.* **1998**, 1315–1316.

[28] H. E. Blackwell, D. J. O'Leary, A. K. Chatterjee, R. A. Washenfelder, D. A. Bussmann, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 58–71.

[29] In fact, we were able to isolate a small amount of open chain tetramer **37** after catalytic hydrogenation of the dimeric unsaturated linear precursor.



37

Received: November 14, 2001 [F3688]