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β-Methyl-2-amino-2,3-didesoxyribofuranoside, a Novel Building Block for Backbone Modified Antisense Oligonucleotides

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Summary. A synthesis of the amino sugar 2-amino-2,3-didesoxyribose is described. Starting from *D*-glucosamine, β-methylfuranoside was obtained in eight steps in 20% yield. This carbohydrate is a novel building block for nucleosides and for backbone modified antisense oligonucleotides with 2′–5′ amide linkages.

Keywords. Amino sugar; Carbohydrates; Oligonucleotides; Ribose derivatives.

Introduction

The antisense principle is based on the specific recognition of a single gene by an antisense oligonucleotide, which inhibits the translation by selective pairing to the complementary strand [1]. The *RNA* strand of a duplex with *DNA* is cleaved by the nuclease *RNA*se H. The antisense *DNA* strand is not degraded and thus can multiply its effect.

Natural oligonucleotides exhibit poor stability against nucleases and thus cannot be used as therapeutic agents. Therefore, modifications have been introduced to enhance the efficacy of oligonucleotides. Backbone modifications gave rise to the first generation of antisense drugs. Phosphorothioates were found to have advantageous properties. Many antisense drugs now in clinical trials belong to this group [2]. Many other backbone modified antisense oligonucleotides were synthesized and tested [3, 4]. Backbone modifications with phosphorous include dithioates, methylphosphonates, phosphoroamidates, and phosphoroamidimates. Other modifications, such as ether, amine, or amide linkages are more stable against degradation. With peptide nucleic acids, both ribose and phosphate backbone are replaced by polyamide chains [5]. The result is an achiral and neutral backbone with a high hybridisation affinity to complementary nucleic acids. As a drawback, the pharma-

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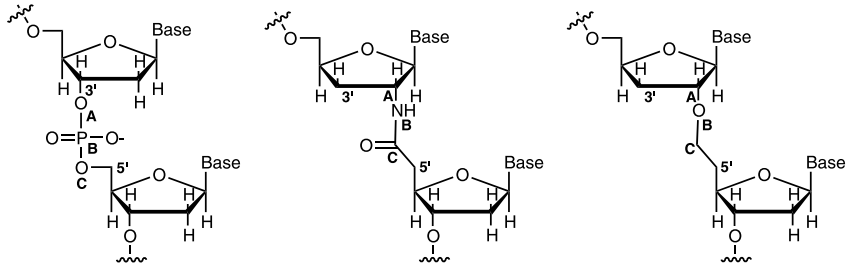


Fig. 1. Structure of natural *DNA* (left), and oligonucleotides with 2′-5′-amide (middle) or ether linkages (right); the distance between carbon 3′ and 5′ is indicated by the letters A, B, and C

cokinetic properties of this type of antisense compounds are unfavourable [6]. Gapmere oligonucleotides are modified at the 3′ and 5′-terminus (wings) and exhibit an unmodified region in between (gap) [7]. This unmodified region is sufficient to activate *RNA*se H, while the terminal modifications provide good stability against enzymatic degradation, which is effected mainly by exonucleases.

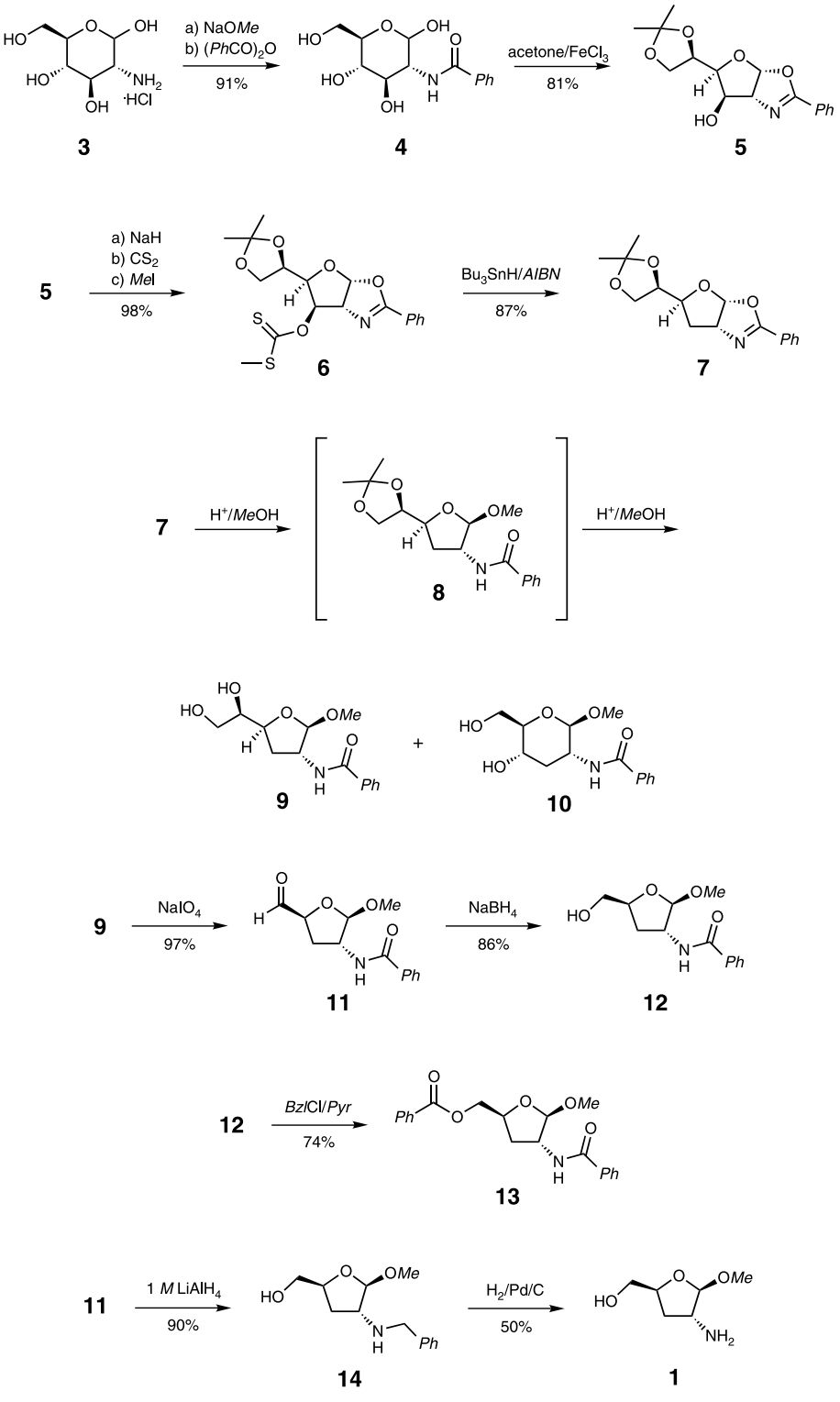
Molecular modelling studies revealed that a 2′–5′ linkage via ether, ester, or amides leads to structures that should be able to hybridise to the corresponding sense strand [8]. With an equal number of atoms in the structural repeating unit, the number of bridging atoms between the rings is reduced by one to redeem for the longer distance within the sugar ring. In vitro experiments with dinucleotides of this type connected *via* an ether linkage revealed that this hitherto undescribed type of structural modification of a nucleic acid is able to undergo triple helix formation with natural oligonucleotides.

An amide backbone modified oligonucleotide (Fig. 1) of the same type should allow a more straightforward synthesis by polyamide formation and was therefore considered to be an attractive antisense modification.

In general, two different approaches may be used for the synthesis of ''sugar modified'' nucleoside building blocks for oligonucleotides: Modification of each compound proceeding from the four natural nucleosides or synthesis of the modified sugar with subsequent nucleosidation reaction, as described by *Vorbrüggen* et al. [9, 10]. With the latter strategy being chosen due to its access to a greater structural diversity concerning the choice of the base, the present paper describes the synthesis of the amino sugar β-methyl-2-amino-2,3-didesoxyribofuranoside (**1**), which has not yet been described, useful as sugar building block for synthesis of backbone modified oligonucleotides.

Results and Discussion

We decided to proceed from the easily available *D*-glucosamine (**2**), since, on the one hand, the configuration of all relevant asymmetric carbon atoms was as required and, on the other hand, there was no need for introduction of the amino group. Our strategy was to reduce the number of carbon atoms to five by diol cleavage. After releasing the base from commercially available *D*-glucosamine-HCl (**3**), the amino function was benzoyl-protected according to *Inouye* et al. [11] to give **4**. This sugar was reacted with acetone and *Lewis* acid to form phenyloxazoline **5** [12], which is


a) NaOMe
b) (PhCO)2O
91%
acetone/FeCl3
81%
3
4
5
a) NaH
b) CS2
c) MeI
98%
Bu3SnH/AIBN
87%
6
7
H+/MeOH
8
H+/MeOH
9
10
NaIO4
97%
NaBH4
86%
11
12
BzlCl/Pyr
74%
13
1 M LiAlH4
90%
H2/Pd/C
50%
14
1

Scheme 1

the key intermediate in the reaction sequence, because the glucosamine exhibits already the desired furanose ring and all reactive groups are protected with exception of the hydroxy group in position 3. This hydroxy group was subsequently removed *via* a two step procedure as first described by *Barton* [13]. In the first step the free hydroxy group was activated using sodium hydride and then transformed to the corresponding dithiocarbonate **6** by reaction with carbon disulfide and methyl iodide. Radical reaction of **6** with tributyltin hydride, activated by *AIBN* (α,α'-azoisobutyronitrile) yielded the deoxygenated product **7** (Scheme 1).

Treatment of the reduced compound **7** with toluenesulfonic acid did not only open the 5,6-dioxolane ring, but also the phenyloxazoline moiety. This could not be avoided, since the oxazoline proved to be more acid labile than the acetonide, a fact that was also observed by other authors for phenyloxazoline **5** [14]. When an insufficient amount of toluenesulfonic acid was used, considerable quantities of **8**, with intact acetonide moiety but opened oxazoline were formed. Traces of water present in the reaction mixture (toluenesulfonic acid was used as a monohydrate) prompted the formation of a small amount of the corresponding pyranoside derivative **10**, along with the desired deprotected ribofuranoside **9**, which was the major product (Scheme 1). These two compounds could easily be separated by flash chromatography. The structures of these isomers, originally assigned by the ^{13}C NMR spectra, were confirmed by 2D NMR experiments. The pyranoside **10** exhibits a pronounced upfield shift of its carbon atom 4 in ^{13}C NMR spectroscopy in comparison to furanoside **9** as well as characteristic changes in shifts of carbons 1, 2, 5, and the methoxy function. Upon standing at room temperature in aqueous solution of toluenesulfonic acid, furanoside **9** showed complete conversion to the pyranoside form within one hour.

Malaprade reaction of **9** with sodium periodate in a solution of aqueous methanol gave ribose derivative **11** in excellent yield (Scheme 1). Aldehyde **11** was reduced by sodium borohydride to give ribofuranoside **12**. For nucleosidation, the 5-hydroxy function was protected as the benzylester using benzyl chloride in pyridine yielding **13**.

Full deprotection of the amino sugar was achieved in a two step procedure. Reduction of aldehyde **11** using lithium aluminium hydride in *THF* not only reduced the aldehyde, but also the benzoyl group to yield benzylamine **14**. Hydrogenolysis with palladium on charcoal cleaved the benzylamine to give the fully deprotected title compound **1**.

In conclusion, we found a good synthetic way to prepare the novel amino sugar **1** resulting in an overall yield of 20%. 2′-Amino-2′,3′-didesoxyuridine has been synthesized starting form uridine by two different synthesis sequences in an overall yield of 7% [18] and 4% [19]. 2′-Amino-2′,3′-didesoxyadenosine was prepared after similar procedures starting from adenosine [18, 20, 21]. By our method, not only natural 2′-amino-2′-desoxynucleosides can be prepared, but also nucleosides containing ‘‘artifical’’ nucleobases.

Experimental

Melting points were measured on a *Kofler* melting point apparatus. Anhydrous solvents were obtained as follows: *THF* and toluene were refluxed on Na and then distilled, methanol was heated over

magnesium methoxide and then distilled. NMR spectra were recorded on a Bruker Spectrospin 200 MHz or a Varian Unity 300 MHz instrument. Shifts are reported relative to the solvent peak ($CHCl_3$ in $CDCl_3$: $\delta = 7.26$ and 77.00 ppm, *DMSO* in *DMSO*-d_6: $\delta = 2.49$ and 39.50 ppm). Thin layer chromatography (TLC) was performed using silica gel 60-F_{254} precoated aluminum plates by Merck. Column chromatography was performed with Merck silica gel 60. Elemental analyses were done by *J. Theiner* (Mikroanalytisches Laboratorium of the University of Vienna). Results agreed favourably with the calculated values.

N-Benzoylglucosamine (**4**, $C_{13}H_{17}NO_6$)

Sodium methoxide (14.61 g, 250 mmol) was dissolved in 450 cm^3 of methanol and 53.90 g of *D*-glucosamine hydrochloride (250 mmol) were added. After 10 min the precipitated NaCl was filtered off and washed with methanol. The filtrate was treated with 59.12 g of benzoic acid anhydride (275 mmol) under stirring. After 30 min, in which precipitation already started, the mixture was cooled for 24 h. Filtration gave 64.43 g of *N*-benzoylglucosamine (**4**) (91%) as a white solid. Mp 204–205°C (Ref. [11] 204–206°C).

2-Phenyl-4,5-(5,6-isopropylidene-D-glucofurano)-1,3-oxazoline (**5**, $C_{16}H_{19}NO_5$)

N-Benzoylglucosamine (**4**) (34 g, 120 mmol) was suspended in 500 cm^3 of acetone. Iron(III)chloride (40 g, 247 mmol) was added under stirring and the resulting solution was heated to reflux for 20 min. After cooling to 0°C 68 g of diethylamine (930 mmol) were slowly added together with 350 cm^3 of acetone followed by a solution of 57 g of Na_2CO_3 in H_2O. Acetone and diethylamine were evaporated and the resulting solution was extracted with 4×300 cm^3 of ether. The organic phases were dried and the solvent was evaporated. The residue was **5** (29.03 g, 79%), pure enough to be used for the subsequent reaction. Crystallization from ether gave **5** as a white solid. Mp 160–161°C (Ref. [15] 159–160°C); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.01$–7.90 (m, 2Ar-H), 7.59–7.35 (m, 3Ar-H), 6.37 (d, $J = 5.1$ Hz, H-1), 4.71 (d, $J = 5.1$ Hz, H-2), 4.55 (d, $J = 2.8$ Hz, H-3), 4.36 (ddd, $J = 5.0$, 6.1, and 7.7 Hz, H-5), 4.16 (dd, $J = 6.1$ and 8.6 Hz, H-6), 3.98 (dd, $J = 5.0$ and 8.6 Hz, H-6′), 3.79 (dd, $J = 2.8$ and 7.7 Hz, H-4), 2.17 (s, OH), 1.39 (s, CH_3), 1.35 (s, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 165.40$ (C=N), 132.06 (Ar C-4), 128.47 (Ar C-2,6), 128.42 (Ar C-3,5), 126.42 (Ar C-1), 109.40 (CMe_2), 107.14 (C-1), 81.91 (C-4), 78.58 (C-2), 74.69 (C-3), 72.79 (C-5), 67.32 (C-6), 26.68 (CH_3), 25.10 (CH_3) ppm.

S-Methyl-O-[2-phenyl-4,5-(5,6-isopropylidene-D-glucofurano)-1,3-oxazolinyl] dithiocarbonate (**6**, $C_{18}H_{21}NO_5S_2$)

With exclusion of moisture 15.0 g of **5** (49 mmol) were dissolved in 150 cm^3 of dry *THF* and the mixture was cooled to 0°C. Under vigorous stirring 1.5 g of NaH (59 mmol) were added, followed 15 min later by 500 mg of imidazole (7.3 mmol). After 2 h of stirring at 20°C, 4.8 cm^3 of CS_2 (6 g, 79 mmol) and another 15 min later 4.2 cm^3 of *Me*I (9.6 g, 68 mmol) were added and stirring was continued for 15 min. After addition of 100 cm^3 of ether the mixture was washed with 3×100 cm^3 of H_2O and brine. Workup of the organic phase yielded 19.0 g of **6** (97%) as a brownish solid which was used without purification for the next reaction. An analytical sample was crystallized from ether, giving **6** as a white solid. Mp 125–128°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.05$–7.96 (d, $J = 6.9$ Hz, 2Ar-H), 7.58–7.37 (m, $J = 1.6$ Hz, 3Ar-H), 6.33 (d, $J = 5.2$ Hz, H-1), 6.11 (d, $J = 2.8$ Hz, H-3), 4.90 (d, $J = 5.2$ Hz, H-2), 4.34 (m, $J = 5.6$ and 12.6 Hz, H-5), 4.05 (m, H-4, H-6, H-6′), 2.63 (s, SCH_3), 1.37 (s, CH_3), 1.31 (s, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 214.25$ (OCS_2), 165.96 (C=N), 132.13 (Ar C-4), 128.64 (Ar C-3,5), 128.36 (Ar C-2,6), 109.29 (CMe_2), 106.54 (C-1), 83.96 (C-3), 80.36 (C-4), 76.34 (C-2), 72.32 (C-5), 66.63 (C-6), 26.64 (CH_3), 25.09 (CH_3), 19.30 (SCH_3) ppm.

2-Phenyl-4,5-(3-desoxy-5,6-isopropylidene-D-glucofurano)-1,3-oxazoline (**7**, $C_{16}H_{19}NO_4$)

Carbon disulfide ester **6** was dissolved in 100 cm^3 of dry toluene and the mixture was heated under Ar to 80°C. Tributyl tin hydride (3.5 cm^3, 3.8 g, 13 mmol) was injected slowly over a period of 30 min and 110 mg of *AIBN* (0.67 mmol) were added. After heating for 17 h a control TLC (petroleum ether: diethyl ether = 1:1) showed no remaining educt ($R_f = 0.95$) and a main product ($R_f = 0.46$). The solvent was removed by evaporation and the residue was purified by column chromatography (petroleum ether:diethyl ether = 3:1–1:1) giving 3.18 g of the deoxygenated oxazoline **7** (87%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.02$–7.91 (dd, $J = 0.7$ and 7.5 Hz, 2Ar-H), 7.55–7.35 (m, 3Ar-H), 6.24 (d, $J = 5.1$ Hz, H-1), 4.84 (dd, $J = 5.1$ and 7.5 Hz, H-2), 4.18–4.02 (m, H-5, H-6), 3.97–3.85 (m, H-4), 3.84–3.74 (m, H-6′), 2.37 (dd, $J = 4.5$ and 13.0 Hz, H-3), 2.03 (ddd, $J = 7.5$, 10.5, and 13.1 Hz, H-3′), 1.38 (s, CH_3), 1.34 (s, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 164.13$ (C=N), 131.70 (Ar C-4), 128.33 (Ar C-2,3,5,6), 126.79 (Ar C-1), 109.66 (CMe_2), 107.35 (C-1), 78.93 (C-4), 76.36 (C-5), 71.42 (C-2), 67.03 (C-6), 34.68 (C-3), 26.36 (CH_3), 25.10 (CH_3) ppm.

Acid Catalysed Hydrolysis of 2-Phenyl-4,5-(3-desoxy-5,6-isopropylidene-D-glucofurano)-1,3-oxazoline (**7**)

Oxazoline **7** (10 g, 34.6 mmol) was dissolved in 300 cm^3 of dry methanol and 250 mg of *p*-toluenesulfonic acid (1.32 mmol) were added. The mixture was stirred under Ar at 20°C for 22 h at which time on a control TLC (dichlormethane:methanol = 95:5) a third spot ($R_f = 0.06$) appeared. Starting product can be seen on this TLC at $R_f = 0.62$ and product **9** at $R_f = 0.10$. The reaction was quenched by adding $NaHCO_3$. After filtration and evaporation of the solvent the residue was purified by column chromatography (dichlormethane:methanol = 96:4, after elution of starting product 94:6). Evaporation of the corresponding fractions gave 7.25 g of deprotected **9** (75%), 2.1 g of unreacted **7**, and 400 mg of glucopyranoside **10** (4%).

β-Methyl-2-benzoylamino-2,3-didesoxy-D-glucofuranoside (**9**, $C_{14}H_{19}NO_5$)

White solid, mp 143–144°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.48$ (d, $J = 6.0$ Hz, NH), 7.92–7.78 (m, 2Ar-H), 7.60–7.38 (m, 3Ar-H), 4.80 (s, H-1), 4.25 (m, H-2, H-5), 3.59 (m, H-6), 3.43 (m, H-6′), 3.37 (m, H-4) 3.24 (s, OCH_3), 2.28–2.00 (m, H-3, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 166.68$ (N–C=O), 134.17 (Ar C-1), 131.31 (Ar C-4), 128.18 (Ar C-3,5), 127.54 (Ar C-2,6), 107.72 (C-1), 79.28 (C-5), 75.16 (C-4), 63.78 (C-6), 55.97 (C-2), 53.87 (OCH_3), 31.57 (C-3) ppm.

β-Methyl-2-benzoylamino-2,3-didesoxy-D-glucopyranoside (**10**, $C_{14}H_{19}NO_5$)

White solid, mp 175–178°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.35$ (d, $J = 8.5$ Hz, NH), 7.85–7.78 (m, 2Ar-H), 7.53–7.42 (m, 3Ar-H), 4.95 (d, $J = 5.3$ Hz, OH-4), 4.53 (t, $J = 6.0$ Hz, OH-6), 4.38 (d, $J = 8.3$ Hz, H-1), 3.84 (m, H-2), 3.70 (ddd, $J = 2.0$, 6.0, and 11.6 Hz, H-6), 3.48 (dt, $J = 11.6$ and 6.0 Hz, H-6′), 3.40 (dt, $J = 4.6$ and 9.9 Hz, H-4), 3.35 (s, OCH_3), 3.16 (ddd, $J = 2.0$, 6.0, and 7.0 Hz, H-5), 2.06 (m, H-3), 1.54 (q, $J = 12.0$ Hz, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 165.61$ (N–C=O), 134.60 (Ar C-1), 131.23 (Ar C-4), 128.29 (Ar C-3,5), 127.24 (Ar C-2,6), 103.22 (C-1), 80.98 (C-5), 64.43 (C-4), 61.15 (C-6), 55.71 (OCH_3), 48.88 (C-2), 37.78 (C-3) ppm.

β-Methyl-2-benzoylamino-2,3,5-tridesoxy-5-oxo-D-ribofuranoside (**11**, $C_{13}H_{15}NO_4$)

To a stirred solution of 8.0 g of **9** (28.5 mmol) in 300 cm^3 of aqueous methanol (67%) 120 cm^3 of an aqueous solution of 6.4 g of $NaIO_4$ (29.9 mmol) were added. The mixture was stirred at 20°C for 1 h. The precipitated $NaIO_3$ was filtered off and methanol was evaporated. The aqueous phase was

extracted three times with ethyl acetate, the organic phase was washed with brine, dried over $NaSO_4$, and the solvent removed in vacuo yielding 6.9 g of **11** (97%) as a yellowish syrup which crystallized after standing at rt for a few days. Mp 70–72°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 9.64$ (d, $J = 1.8$ Hz, H-5), 7.83–7.70 (m, 2Ar-H), 7.58–7.36 (m, 3Ar-H), 6.28 (d, $J = 6.3$ Hz, NH), 5.04 (s, H-1), 4.64–4.51 (m, H-2, H-4), 3.45 (s, OCH_3), 2.54 (dt, $J = 7.0$ and 13.9 Hz, H-3), 2.16 (ddd, $J = 1.0$, 8.8, and 13.9 Hz, 1H, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 202.00$ (C-5), 167.43 (N–C=O), 133.64 (Ar C-1), 131.74 (Ar C-4), 128.47 (Ar C-3,5), 126.96 (Ar C-2,6), 108.65 (C-1), 81.38 (C-4), 55.64 (OCH_3), 55.16 (C-2), 30.80 (C-3) ppm.

β-Methyl-2-benzoylamino-2,3-didesoxy-D-ribofuranoside (**12**, $C_{13}H_{17}NO_4$)

Aldehyde **11** (1.6 g, 6.4 mmol) was dissolved in 30 cm^3 of ethanol and 250 mg of sodium borohydride (6.6 mmol) were added. After 3 h of stirring at 20°C the solvent was evaporated and the residue was dissolved in ethyl acetate. The organic phase was washed with H_2O and brine, dried over $NaSO_4$, and the solvent was removed yielding 1.38 g of **12** (86%) as a pale syrup. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.73$ (d, $J = 7.2$ Hz, Ar-H-2,6), 7.41 (dd, Ar-H-3,4,5), 6.52 (d, $J = 6.9$ Hz, NH), 4.88 (s, H-1), 4.57 (t, $J = 6.9$ Hz, H-2), 4.47 (m, H-4), 3.72 (bd, $J = 11.5$ Hz, H-5), 3.52 (dd, $J = 5.8$ and 11.5 Hz, H-5′), 3.39 (s, OCH_3), 2.63 (bs, OH), 2.31 (ddd, $J = 1.5$, 6.8, and 13.6 Hz, H-3), 1.94 (ddd, $J = 0.9$, 6.8, and 13.6 Hz, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 167.59$ (N–C=O), 133.69 (Ar C-1), 131.33 (Ar C-4), 128.13 (Ar C-3,5), 126.90 (Ar C-2,6), 107.81 (C-1), 80.15 (C-4), 65.28 (C-5), 56.07 (C-2), 54.55 (OCH_3), 30.59 (C-3) ppm.

β-Methyl-5-benzoyl-2-benzoylamino-2,3-didesoxy-D-ribofuranoside (**13**, $C_{20}H_{21}NO_5$)

To a solution of 1 g of **12** (3.98 mmol) in dry pyridine, cooled to 0°C, 750 mg of benzoic acid chloride (5.34 mmol) were added. The mixture was allowed to reach rt and was stirred for 17 h. After removal of solvent in vacuo, the residue was purified by flash chromatography (petrol ether:ethyl acetate = 2:1). After unreacted benzoic acid chloride, the desired product **13** eluted. Drying of the appropriate fractions afforded 1.04 g of **13** (74%) as a pale yellow syrup. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 8.08$ (dd, $J = 1.4$ and 6.9 Hz, Ar-H-2,6; benzylester), 7.75 (dd, $J = 1.5$ and 6.6 Hz, Ar-H-2,6; benzylamide), 7.61–7.36 (m, 6Ar-H), 6.36 (d, $J = 7.3$ Hz, NH), 4.95 (s, H-1), 4.65 (m, H-2, H-4), 4.44 (dd, $J = 4.0$ and 11.5 Hz, H-5), 4.32 (dd, $J = 6.8$ Hz, H-5′), 3.37 (s, OCH_3), 2.33 (ddd, $J = 6.1$, 8.9, and 13.4 Hz, H-3), 2.13 (dd, $J = 7.4$ Hz, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 167.33$ (N–C=O), 166.27 (O–C=O), 133.86 (Ar-C-1; benzylamide), 133.02 (Ar-C-4; benzylester), 131.56 (Ar-C-4; benzylamide), 129.76 (Ar-C-1; benzylester), 129.55 (Ar-C-2,6; benzylester), 128.34 und 128.27 (Ar-C-3,5; benzylester and benzylamide), 126.95 (Ar-C-2,6; benzylamide), 107.90 (C-1), 76.76 (C-4), 67.58 (C-5), 55.94 (C-2), 54.47 (OCH_3), 32.13 (C-3) ppm.

β-Methyl-2-benzylamino-2,3-didesoxy-D-ribofuranoside (**14**, $C_{13}H_{19}NO_3$)

Aldehyde **11** (400 mg, 1.6 mmol) was dissolved in 3.5 cm^3 of a 1 *M* solution of $LiAlH_4$ in *THF* and the mixture was refluxed under Ar for 17 h. The reaction was quenched by dropwise addition of H_2O until no more H_2 evolved. Ethyl acetate was added and the precipitated Al_2O_3 was filtered off and washed with ethyl acetate. Evaporation of the organic solvents gave 340 mg of **14** (90%) as a yellowish syrup. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.31$ (bs, 3Ar-H), 4.81 (s, H-1), 4.48 (ddt, $J = 2.8$, 4.6, and 7.5 Hz, H-4), 3.80 (s, $PhCH_2$), 3.72 (dd, $J = 2.8$ and 11.7 Hz, H-5), 3.47 (dd, $J = 4.6$ and 11.8 Hz, H-5′), 3.37 (s, OCH_3), 3.33 (dd, $J = 2.2$ and 6.6 Hz, H-2), 2.14 (ddd, $J = 6.6$, 7.5, and 13.1 Hz, H-3), 1.81 (ddd, $J = 2.1$, 7.5, and 13.1 Hz, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 139.57$ (Ar C-1), 128.36 and 128.04 (Ar C-3,5 and Ar C-2,6), 127.05 (Ar C-4), 108.56 (C-1), 80.41 (C-4), 65.32 (C-5), 63.73 (C-2), 54.88 (OCH_3), 51.92 ($PhCH_2$), 31.41 (C-3) ppm.

β-Methyl-2-amino-2,3-didesoxy-D-ribofuranoside (**1**, $C_6H_{13}NO_3$)

Benzyl derivative **14** (600 mg, 2.5 mmol) was dissolved in 60 cm^3 of methanol and 330 mg of 10% palladium on charcoal (0.31 mmol) were added. The mixture was stirred under H_2 (4 bar) for 17 h. The catalyst was filtered off over Celite® and the filtrate was evaporated giving 186 mg of **1** (50%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.65$ (s, H-1), 4.47 (m, H-4), 3.69 (dd, $J = 3.0$ and 11.7 Hz, H-5), 3.45 (dd, $J = 5.1$ and 11.7 Hz, H-5′), 3.43 (m, H-2), 3.35 (s, OCH_3), 2.12 (m, H-3), 1.67 (ddd, $J = 1.2$, 7.3, and 12.9 Hz, H-3′) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 110.46$ (C-1), 79.99 (C-4), 65.40 (C-5), 57.14 (C-2), 54.65 (OCH_3), 33.38 (C-3) ppm.

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