

Synthesis of 3'-azido- and 3'-amino-3'-deoxyadenosine in both enantiomeric forms

Oliver Botta, Elisabeth Moyroud, Cinta Lobato and Peter Strazewski*

Institute of Organic Chemistry, University of Basel, St. Johannis-Ring 19, CH – 4056 Basel, Switzerland

Received 22 July 1998; accepted 30 August 1998

Abstract: Aminosugar nucleosides are important bioactive molecules of which puromycin, a derivative of 3'-amino-3'-deoxyadenosine, is one of the most important examples. Some azidosugar nucleosides, the synthetic precursors of the corresponding aminosugar compounds, are known to be active against HIV reverse transcriptase. We are interested in comparing the bioactivity of D- and L-enantiomers of such nucleosides. Here, the synthesis of both D- and L-enantiomers of 3'-azido- and 3'-amino-3'-deoxyadenosine, respectively, is described. It begins with the introduction of the nitrogen functionality through a substitution reaction with inversion at C-3 of a D- or L-xylose derivative, respectively. The azidosugar is converted into an appropriate glycosyl donor which is submitted to a glycosidation reaction according to *Vorbrüggen*. Deprotection affords 3'-azido-3'-deoxy-D/L-adenosine, our potentially antiviral target compounds, and reduction of the azido substituent leads to the aminosugar target molecules. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: nucleosides; glycosidation; amino sugars; azides

Introduction

Aminosugar nucleosides are known to possess strong antibacterial, anticancer and biosynthetic inhibitory properties.^{1,2} One of the most important examples of this class of compounds is puromycin, a molecule which mimics the charged 3'-terminus of aminoacylated transfer RNA and is a strong acceptor for the peptidyl tRNA site of the ribosome. In addition, it is known that the nucleoside moiety of puromycin, 6-N,N-dimethyl-3'-amino-3'-deoxyadenosine, shows activity against *Trypanosoma equiperdum*.³

3'-Azido-3'-deoxythymidine (AZT), the first licensed drug for the treatment of AIDS patients, exhibits the most potent inhibitory activity against human immunodeficiency virus (HIV) replication. However, AZT suffers from a rather short half-life in the body and exhibits side effects. Other 3'-azido- and 3'-amino-2',3'-dideoxyribonucleosides, among a vari-

ety of nucleoside derivatives, have been synthesised and tested,⁴ but neither 3'-azido- nor 3'-amino-3'-deoxyribonucleosides. Furthermore it is known that L-nucleotides cannot be incorporated into oligonucleotides by RNA or DNA polymerases due to the high stereoselectivity of these enzymes, and that they are stable in biological fluids.⁵ There is a chance that the stereoselectivity of retroviral reverse transcriptases against unnaturally configured nucleotides is considerably lower than that of human enzymes. Therefore, L-nucleosides should be evaluated for their potential inhibitory properties.

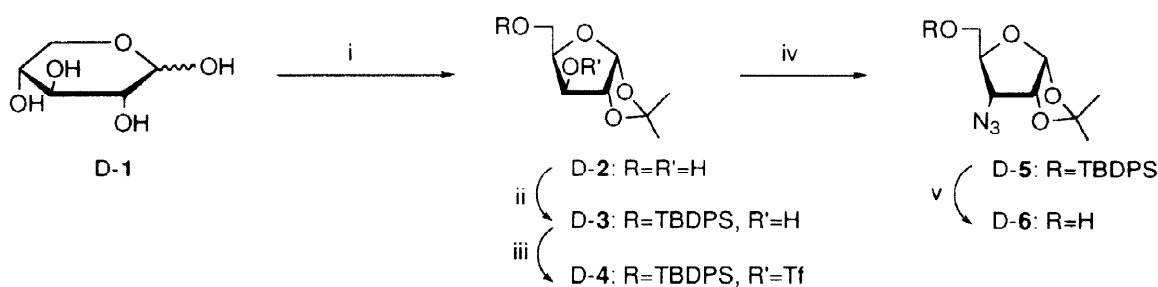
There are two major strategies for the synthesis of sugar-modified nucleosides: *i*) modifications on the intact nucleosides,^{4,6-10} and *ii*) coupling of appropriately modified glycosyl donors with heterocyclic bases.¹¹⁻¹⁸ The first strategy is usually selected for point modifications on the sugar moiety. Synthetic routes are usually straightforward and include extensive use of a wide range of protecting groups in combination with oxidation/reduction or substitution reactions. The use of the second strategy is crucially dependent on the successful turnover of the glycosidation reaction, but has three major advantages: a) the number of useful bases is not limited to those of commercially available nucleosides,¹⁹⁻²⁴ b) the degree of complexity being introduced into the glycoside moiety can be considerably higher as shown by the methods chosen for the synthesis of natural products with a nucleosidic basic structure²⁵ or of complex nucleoside antibiotics,²⁶ c) the synthesis of L-nucleosides becomes possible.

Results and Discussion

The synthesis of 3'-amino-3'-deoxyadenosine is described for the naturally configured D-isomer since most of the procedures were elaborated in the D series. After the synthetic route had been found, the synthesis of the L-isomer was optimized and slightly adapted.

Starting from commercially available D-xylose (D-1), the first synthetic step involves the acetonation of the sugar to form 1,2-O-isopropylidene- α -D-xylofuranose (D-2), thus to convert xylopyranose into a furanose derivative.²⁷ Since acetone is the solvent, diacetonation to 1,2;3,5-di-O-isopropylidene- α -D-xylofuranose can not be avoided. Treating this compound with 0.12 M HCl-solution for 40 minutes at room temperature leads to the mono-acetonated compound, therefore increasing the overall yield of this reaction to 70% (Scheme 1).

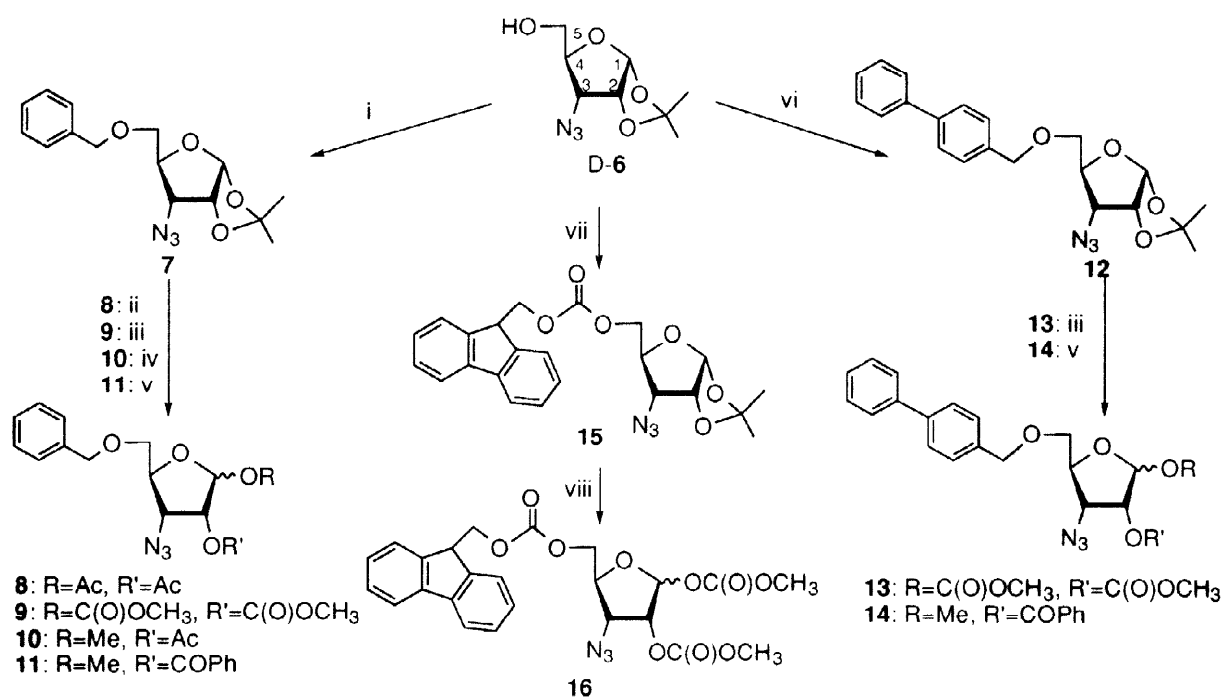
Scheme 1



(i) acetone, cat. H₂SO₄, rt, 3h, D:70%, L:80% (ii) TBDPSCl, imidazole, DMF, rt,3h, D:60%, L:97% ; (iii) (F₃CSO₂)₂O, pyridine, CH₂Cl₂, -10°C, 15min.; (iv) NaN₃, pyridine, DMF, rt, 7 days, D:56%, L: 54%; (v) TBAF, THF; rt, 2h, D:95%, L:87%.

After fixation of the furanose configuration through selective protection of the primary hydroxyl group with the *tert*-butyldiphenylsilyl (TBDPS) (\rightarrow D-3), the inversion at C-3 was carried out in two steps: first, the hydroxy group was activated as a triflate using trifluoromethanesulfonic anhydride. Intermediate D-4 was used in the next step without purification since analysis by $^1\text{H-NMR}$ spectroscopy showed sufficient purity. In the second step, the sulfonate was replaced by an azido group using sodium azide leading to D-5 with inverted configuration at C-3. This reaction needed a very long reaction time, because the mixture could not be heated due to an undesired elimination reaction resulting in a 3,4-unsaturated compound and triflic acid.^{15,28} The yield of the desired reaction product is crucially dependent on the ratios of the reactants, especially the amount of pyridine to be used. Using two equivalents of pyridine, the appearance of the 3,4-elimination product was observed in up to 50% of the total yield. In order to suppress this side-reaction, the amounts of pyridine were reduced down to one or 1.5 equivalents. Under these conditions, however, the deprotection of the TBDPS-group at C(5) on both D-5 and the elimination product appeared to become another side reaction due the development of free triflic acid. The deprotection product of D-5 is D-6, which was the target of our next reaction step, and was therefore not lost. D-5 was desilylated with fluoride to give D-6 in good yields.

Scheme 2



(i) 1) NaH, THF, 65°C; 2) BnBr, TBAI, THF, rt, o/n, 85% overall (ii) 1) 75% HCOOH, 60°C, 1h; 2) Ac₂O, pyridine, rt, 2h, 75% overall; (iii) 1) 75% HCOOH, 60°C, 1h; 2) CH₃OCOC(=O)Cl, NEt₃, MeCl₂, 0°C, 2h, **9**: 83% overall, **13**: 98% overall; (iv) 1) MeOH, cat. H₂SO₄, 4°C, 2 days; 2) Ac₂O, pyridine, rt, o/n, 59% overall; (v) 1) MeOH, cat. H₂SO₄, 4°C, 2 days; 2) PhCOCl, pyridine, cat. DMAP, rt, o/n, **11**: 83% overall, **14**: 83% overall; (vi) 1) NaH, THF, 65°C; 2) 4-(Chloromethyl)-biphenyl, TBAI, THF, rt, o/n, 75% overall; (vii) FMOCCl, pyridine, rt, 1h, 96%; (viii) 1) 75% HCOOH, 60°C, 5h; 2) CH₃OCOC(=O)Cl, pyridine, 0°C, 1.5h, 43%.

The glycosidation reaction calls for glycosyl donors with stable protecting groups on all hydroxy functions that are not participating in the reaction, an acyl group at the C(2) oxygen atom and a leaving group at C(1).²⁹ In the first approach, the use of a 5-O-protecting group was considered that is stable under glycosidation conditions and that could be removed after forming the nucleoside without affecting the other protecting groups. The benzyl group was introduced in good yield to form **7** which was then converted into the glycosyl donors **8**, **9**, **10** and **11** using modified protocols from refs. 15, 30 and 31 (Scheme 2, the β -anomers were the major products).

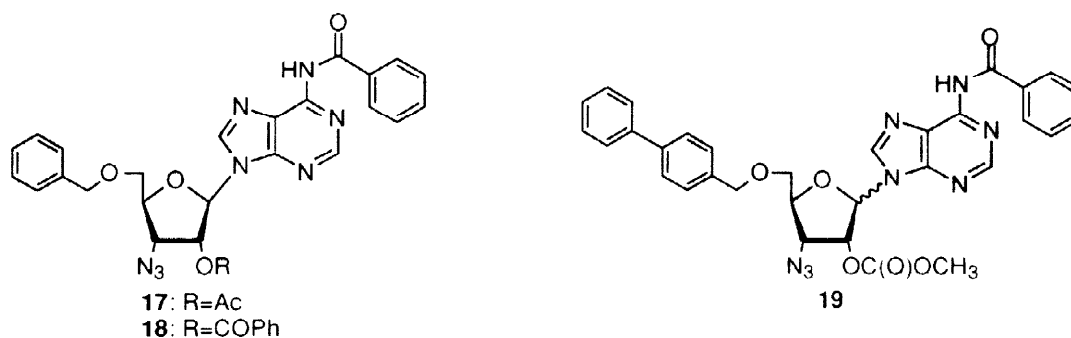
At this stage we considered using other 5-O-protecting groups, since the debenzilation by catalytic hydrogenation can be strongly affected in the presence of amines and the reduction of the azide is expected to proceed faster than the cleavage of the ether.³² Thus, we chose to synthesize other 5-O-protected glycosyl donors featuring two mildly cleavable functionalities: 1) *p*-phenylbenzyl ethers can be cleaved under oxidizing conditions with 2,3-dichloro-5,6-dicyano-1,4-dibenzoquinone (DDQ)³³ or ceric ammonium nitrate (CAN); 2) the 9-fluorenylmethoxycarbonyl (Fmoc) group is used in peptide chemistry and can be cleaved

Table 1: Glycosidation of 6-*N*-benzoyladenine using various glycosyl donors

Entry	Glycoside	Solvent ^{a)}	Catalyst	Temperature (°C)	Time ^{a)} (h)	Yield ^{b)} (%)	Ratio (β/α) ^{a)}
1	8	DCE	TMS-OTf	reflux (84)	3	38	> 95/5
2	9	DCE	TMS-OTf	reflux	17	45	3/1
3	9	CH ₃ CN	TeI ₄	rt->reflux	on.->3	40	3/1
4	9	CH ₃ CN	TeI ₄	reflux (82)	4	38	> 95/5
5	10	CH ₃ CN	TMS-OTf	reflux	3 days	-	-
6	10	DCE	SnCl ₄	reflux	on.	-	-
7	11	DCE	SnCl ₄	reflux	5	22	n.d.
8	11	DCE	TMS-OTf	80	on.	55	> 95/5
9	14	CH ₃ CN	TMS-OTf	65-70	3 days	10	> 95/5
10	13	CH ₃ CN	TMS-OTf	65	23	47	1/9
11	16	CH ₃ CN	TMS-OTf	65	10	-	-
12	16	DCE	TMS-OTf	65	22	-	-

a) Abbreviations: DCE: 1,2-dichloroethane; on.: overnight; rt: room temperature; n.d.: not determined

b) The protocols for entries 4 (\rightarrow **17**), 8 (\rightarrow **18**) and 10 (\rightarrow **19**) are described in the Experimental Part.



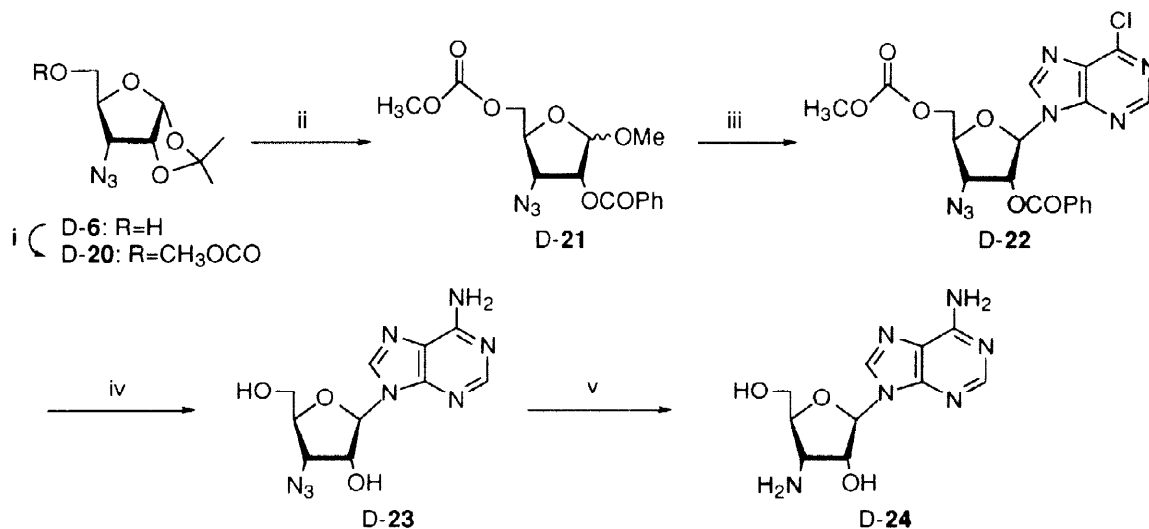
with mild bases like aqueous ammonia, piperidine, morpholine, ethanolamine or fluoride.^{34,35} Following the same protocols as for the benzyl-protected derivatives, the azido-sugars **12** to **16** were synthesised, the β -anomers being the major isomers (Scheme 2).

Having the glycosyl donors **8** - **11**, **13**, **14** and **16** at hand, the synthesis of 3'-azido-3'-deoxy- β -D-adenosine derivatives was carried out using 6-N-benzoyladenine and glycosidation protocols of *Vorbrüggen*¹⁹ and others.^{24,36} The results are summarized in Table 1.

Several conclusions could be drawn: 1) the optimal conditions for glycosidation reactions of different glycosyl donors are idiosyncratic with respect to the protection scheme of the glycosyl donor, especially concerning the solvent and the catalyst (entries 7 and 8); 2) it is possible to obtain anomeric mixtures of the nucleoside although, according to theory, the attack of the base should happen exclusively from the β -side of the sugar (entries 3, 7, 10); 3) the substituent at C-5, although it is far away from the reaction centre, may influence the yield of the glycosidation, possibly due to steric hindrance (entries 11 and 12); 4) heating the reaction mixture higher than 80° C destroys the glycosyl donor, but heating to at least 60° C is necessary to obtain the thermodynamically preferred N(9)-regioisomer of adenosine; 5) 6-N-benzoyladenine persistently produces bad yields in these reactions, especially if the reaction temperature is limited; it would be better to use a more electron-rich aromatic system.

The next steps would have been the selective deprotection of the 5-O-protecting groups. But neither the deprotection of the benzyl group from **18** by catalytic hydrogenation nor the deprotection of the *p*-phenylbenzyl group from **19** with DDQ or CAN gave useful results. Therefore we were forced to develop a new strategy in consideration of the lessons learned above. This new strategy includes: 1) usage of the small methoxycarbonyl function to protect the C-5 hydroxy group; 2) choice of the 1-O-methyl-2-O-benzoyl-combination for the glycosyl donor; 3) replacement of 6-N-benzoyladenine by 6-chloropurine to obtain better yields

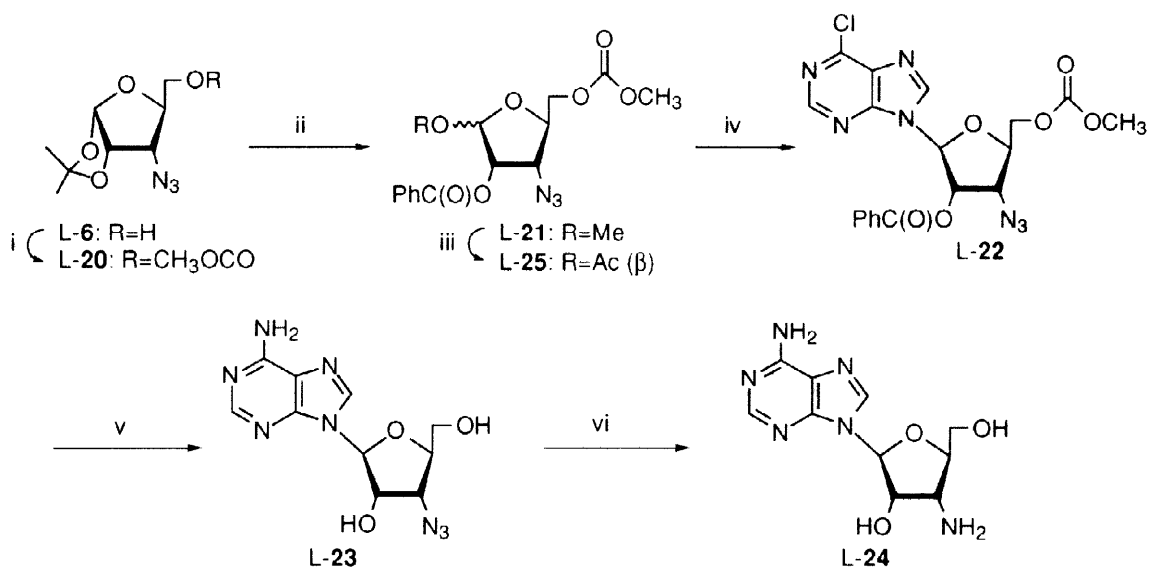
Scheme 3



because of the more electron rich aromatic system, but to retain N(7)/N(9) selectivity on the base. Glycosyl donor D-21 was synthesised from D-6 via the intermediate D-20 followed by the glycosidation to obtain pure β -nucleoside derivative D-22 (Scheme 3). Treating D-22 with ammonia cleaves the protecting groups and replaces chlorine by an amino group.^{37,38} This leads to 3'-azido-3'-deoxy-D-adenosine (D-23) which can easily be converted to 3'-amino-3'-deoxy-D-adenosine (D-24) by catalytic hydrogenation (Scheme 3).

With these results the synthesis of the L-isomer could be started following the same procedures to obtain the glycosyl donor L-22 (Schemes 1, see legend, and 4). Knowing that acetyl is a better leaving group,²² the glycosyl donor L-25 was synthesised. Because of the bad anomeric ratio of the product mixture (β/α 1.5/1), the two anomers of L-25 were isolated. In order to obtain good yields (no reaction of the α -anomer is expected due to the lower reaction temperature of maximal 80°C)³⁹, only the β -anomer of L-25 was submitted to the glycosidation with 6-chloropurine. Under the same conditions as for the pure β -anomer of L-21 (17% L-22), the nucleoside derivative L-22 was obtained in good yield (81%). Ammonia treatment and catalytic hydrogenation furnished 3'-amino-3'-deoxy-L-adenosine (L-24) in 26% overall yield from 6 (Scheme 4).

Scheme 4



(i) methylchloroformate, pyridine, rt, o/n, 92%; (ii) 1) MeOH, cat. H₂SO₄, 4°C, 2 days; 2) PhCOCl, pyridine, cat. DMAP, rt, o/n, 92%; (iii) Ac₂O, AcOH, H₂SO₄, o/n, 4°C, 37% α , 57% β ; (iv) β -L-25, 6-chloropurine, MSTFA, TMS-OTf, 1,2-DCE, 75°C, o/n, 81%; (v) sat. NH₃ in MeOH, 60°C, o/n, 73%; (vi) H₂ (1 atm), Pd/C, EtOH, rt, o/n, 67%.

Conclusion

A new efficient synthesis of both L- and D-enantiomers of 3'-amino-3'-deoxyadenosine was developed including a glycosidation reaction. The optimal conditions for this glycosidation are crucially dependent on the substitution pattern of the glycosyl donor and have to be determined for every individual derivative.

The nucleoside analogues D-23, D-24, L-23 and L-24 will be tested for biological activity.

Experimentals

¹H-NMR spectra were obtained at 300 MHz on a VARIAN Gemini 300 spectrometer using tetramethylsilane as an internal standard. ¹³C-NMR spectra were obtained at 75 MHz using the same internal standard. Mass spectra were obtained on a MAT 312 mass spectrometer using Fast Atomic Bombardment (FAB) ionization method (in *p*-nitrobenzyl alcohol, if not stated otherwise) and positive ion detection. Infrared spectra were recorded on a Perkin-Elmer 1600 Series FTIR Spectrometer. $[\alpha]_D$ -values were obtained on a Perkin-Elmer 141 Polarimeter. Melting points were determined by visual observation on a Kofler block and are corrected. TLC was performed on pre-coated silica gel F₂₅₄ plates with fluorescent indicator. Glycosides and nucleosides were visualised on TLC plates by subsequent spraying with naphthoresorcin and conc. H₂SO₄ solutions in ethanol, respectively, followed by heating. Column chromatography was performed with flash silica gel (35–70 μm) by *Uetikon*. Dry pyridine was obtained by distillation over CaH₂. All other solvents were used as purchased. Abbreviations: PE: petrol ether, TBME: *tert*-butylmethylether; DCE: 1,2-dichloroethane; TBDPSCl: *tert*-butyldiphenylsilyl chloride; TBAF: tetrabutylammonium fluoride; TBAI: tetrabutylammonium iodide; HMDS: hexamethyldisilazane; DMAP: 4-dimethylaminopyridine; MSTFA: N-methyl-N-trimethylsilyltrifluoroacetamide; TMS-OTf: trimethylsilyl trifluoromethanesulfonate.

5-O-*tert*-Butyldiphenylsilyl-1,2-O-isopropylidene- α -D-xylofuranose (D-3). To a solution of 7.4 g (3.9 mmol) 1,2-O-isopropylidene-D-xylofuranose¹⁵ (D-2) and 10.6 g (15.6 mmol) imidazole in 40 ml DMF under argon at 0°C were added 11.8 ml (46.1 mmol) TBDPSCl and the mixture was allowed to react at room temperature for 3 hours. 100 ml TBME and 15 ml H₂O were added and the phases separated. The organic phase was washed twice with water, dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/TBME 6:4) and crystallization from PE 10.0 g (60%) of D-3 were obtained as colorless crystals. *R*_f: 0.43 (PE/TBME 5:5); mp: 92–94°C; ¹H-NMR (CDCl₃): 1.05 (*s*, 9H, C(CH₃)₃); 1.33 (*s*, 3H, CH₃); 1.47 (*s*, 3H, CH₃); 4.03 (*d*, 1H, *J*=2.8, HO-C(3)); 4.10–4.14 (*m*, 3H, H₂C(5), HC(4)); 4.37 (*br t*, 1H, HC(3)); 4.55 (*d*, 1H, ³*J*=3.6, HC(2)); 6.01 (*d*, 1H, ³*J*=3.8, HC(1)); 7.37–7.73 (*m*, 10H, Ph); ¹³C-NMR (CDCl₃): 19.10 (C(CH₃)₃); 26.18 (C(CH₃)₂); 26.69 (C(CH₃)₃); 26.79 (C(CH₃)₂); 26.80 (C(5)); 76.87 (C(4)); 78.37 (C(3)); 85.44 (C(2)); 104.99 (C(1)); 111.50 (C(CH₃)₂); 127.92, 130.05, 131.90, 135.49, 135.69 (C Ph); FAB-MS: 371 ([M-C₄H₉)⁺, 20%), 135 (100%).

5-O-*tert*-Butyldiphenylsilyl-3-O-trifluoromethanesulfonyl-1,2-O-isopropylidene- α -D-xylofuranose (D-4). 4.40 ml (26.7 mmol) Trifluoromethanesulfonic anhydride were added slowly at -10°C to a solution of 10.5 g (24.5 mmol) D-3 and 2.9 ml (23.8 mmol) pyridine in 250 ml CH₂Cl₂. After 15 minutes at -10°C the solution was warmed to room temperature and diluted in 250 ml TBME. This phase was washed with water and 1 M HCl-solution, dried over Na₂SO₄ and evaporated to furnish 12.8 g of an orange oil. ¹H-NMR (CDCl₃): 1.06 (*s*, 9H, C(CH₃)₃); 1.33 (*s*, 3H, CH₃); 1.47 (*s*, 3H, CH₃); 3.88 (*s*, 2H, ³*J*=6.6, H₂C(5)); (*td*, 1H, ³*J*=6.6, ³*J*=2.7, HC(4)); (*d*, 1H, ³*J*=3.6, HC(2)); (*d*, 1H, ³*J*=2.8, HC(3)); (*d*, 1H, ³*J*=3.6, HC(1)); 7.39–7.69 (*m*, 10H, Ph); ¹³C-NMR (CDCl₃): 19.07 (C(CH₃)₃); 26.34 (C(CH₃)₂); 26.55, 26.70 (C(CH₃)₃); 26.98 (C(CH₃)₃); 60.01 (C(5)); 78.83 (C(2)); 82.84

(C(3)); 87.87 (C(4)); 104.58 (C(1)); 113.03 (C(CH₃)₂); 127.82, 129.93, 129.97, 132.87, 135.58 (C Ph)

3-Azido-5-O-tert-butylidiphenylsilyl-3-deoxy-1,2-O-isopropylidene- α -D-ribofuranose (D-5). To a solution of 5.46 g (9.73 mmol) D-4 in 150 ml DMF under argon 2.53 g (38.92 mmol) NaN₃ and 1.18 ml (14.60 mmol) pyridine were added subsequently. The resulting suspension was stirred at room temperature for five days. 300 ml TBME and 60 ml H₂O were added and the aqueous phase was extracted three times. The organic phases were washed with water, dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/TBME 9:1) 2.47 g (56%) of D-5 were obtained as a yellowish solid. R_f: 0.37 (PE/TBME 9:1); mp: 82–86°C; ¹H-NMR (CDCl₃): 1.05 (s, 9H, C(CH₃)₃); 1.39 (s, 3H, CH₃); 1.58 (s, 3H, CH₃); 3.73 (dd, 1H, ³J=4.7, ³J=9.0, HC(3)); 3.84 (dd, 1H, ³J_{5a,4}=2.9, ²J_{5a,5b}=11.8, H_aC(5)); 3.98 (dd, 1H, ³J_{5b,4}=1.9, ²J_{5b,5a}=11.8, H_bC(5)); 4.15 (d"t", 1H, ³J_{4,3}=9.5, HC(4)); 4.75 (t, 1H, ³J=4.1, HC(2)); 5.83 (d, 1H, ³J=3.6, HC(1)); 7.36–7.70 (m, 10H, Ph); ¹³C-NMR (CDCl₃): 19.32 (C(CH₃)₃); 26.49 (C(CH₃)₂); 26.80 (C(CH₃)₃); 60.15 (C(3)); 61.77 (C(5)); 78.44 (C(4)); 80.28 (C(2)); 104.18 (C(1)); 113.05 (C(CH₃)₂); 127.75, 127.80, 129.78, 129.83, 132.90, 133.11, 135.57, 135.66 (C Ph); FAB-MS: 396 ([M-C₄H₉)⁺, 13.2%), 135 (100%); IR (KBr): 2109cm⁻¹ (N₃).

3-Azido-3-deoxy-1,2-O-isopropylidene- α -D-ribofuranose (D-6). To a solution of 2.26 g (4.97 mmol) D-5 in 50 ml THF were added 5.47 ml 1M TBAF-solution in THF. After two hours at room temperature the solution was evaporated to half of the original volume and extracted with H₂O/CH₂Cl₂. The organic fraction was dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/TBME 6:4, then 100% TBME) 1.02g (95%) D-6 were obtained as a colorless oil. R_f: 0.10 (PE/TBME 6:4); ¹H-NMR (CDCl₃): 1.38 (s, 3H, C(CH₃)₂); 1.59 (s, 3H, C(CH₃)₂); 3.61 (dd, 1H, ³J=4.7, ³J=9.6, HC(3)); 3.69 - 3.73 (br d, 1H, ²J_{5a,5b}=12.7, H_aC(5)); 3.98 - 4.03 (d"d", 1H, ²J_{5b,5a}=12.7, H_bC(5)); 4.14 (d"t", 1H, ³J=9.7, HC(4)); 4.76 (t, 1H, ³J=4.2, HC(2)); 5.82 (d, 1H, ³J=3.6, HC(1)); ¹³C-NMR (CDCl₃): 26.10, 26.13 (C(CH₃)₂); 59.14 (C(3)); 59.82 (C(5)); 78.06 (C(4)); 79.93 (C(2)); 103.92 (C(1)); 112.94 (C(CH₃)₂); FAB-MS: 216 ([M+H]⁺, 12.3%), 158 ([M-C₃H₆O]⁺, 73.1%), 43 (100%)

3-Azido-5-O-benzyl-3-deoxy-1,2-O-isopropylidene- α -D-ribofuranose (D-7). 170 mg (3.8 mmol) 55–65% NaH were washed three times with pentane and suspended in 8 ml THF under nitrogen. After addition of a solution of D-6 in 2 ml THF, the mixture was heated to 65°C until the H₂ production has finished. After cooling down to room temperature, 260 mg (0.7 mmol) TBAI and 415 ml (3.5 mmol) freshly distilled benzyl bromide were added and the resulting solution was stirred at room temperature overnight. Evaporation was followed by extraction with H₂O/EtOAc. The organic fraction was dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/TBME 8:2) 800 mg (70%) of D-7 were obtained as a colorless oil. R_f: 0.33 (PE/TBME 8:2); ¹H-NMR (CDCl₃): 1.35 (s, 3H, C(CH₃)₂); 1.60 (s, 3H, C(CH₃)₂); 3.63 (dd, 1H, ³J=4.7, ³J=9.6, HC(3)); 3.68 (dd, 1H, ²J_{5a,5b}=11.4, ³J_{5a,4}=3.8, H_aC(5)); 3.84 (dd, 1H, ²J_{5b,5a}=11.4, ³J_{5b,4}=2.5, H_bC(5)); 4.21 (ddd, 1H, ³J_{4,5b}=2.7, ³J_{4,5a}=3.6, ³J_{4,3}=9.6, HC(4)); 4.62 (d, 1H, ²J=12.2, H_AC); 4.68 (d, 1H, ²J=12.2, H_BC); 4.72 (t, 1H, ³J=4.4, HC(2)); 5.83 (d, 1H, ³J=3.6, HC(1)); 7.29 - 7.36 (m, 5H, Ph); ¹³C-NMR (CDCl₃): 26.42 (C(CH₃)₂); 60.53 (C(3)); 67.60 (C(5)); 73.70 (CH₂Ph);

77.43 (C(4)); 79.90 (C(2)); 104.28 (C(1)); 113.10 (C(CH₃)₂); 127.8, 128.4, 137.7 (Ph); **FAB-MS**: 307 (M+K)⁺, 9.0%; 91 ([C₇H₇]⁺, 100%)

1,2-O-Diacetyl-3-azido-5-O-benzyl-3-deoxy-D-ribofuranose (D-8). 305 mg (1.0 mmol) D-7 were stirred in 12 ml 75% formic acid at 60°C for one hour. The solution was evaporated to dryness and then coevaporated twice with 10ml dioxane and toluene, respectively. The yellow oil was dissolved in 5 ml pyridine, mixed with 3.3 ml (35.0 mmol) Ac₂O and stirred at room temperature for two hours. After addition of 50 g ice, the mixture was extracted with CH₂Cl₂. The organic fractions were washed with sat. NaHCO₃-solution and twice with water, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/TBME 6:4) furnished 263 mg (75%) of the anomeric mixture of D-8 as a colorless oil. R_f: α-anomer: 0.25; β-anomer: 0.38 (PE/TBME 6:4); ¹H-NMR (CDCl₃): 1.96 (s, 3H, C(1)OCOCH₃); 2.17 (s, 3H, C(2)OCOCH₃); 3.60-3.73 (m, 2H, H₂C(5)); 4.15-4.28 (m, 2H, HC(4), HC(3)); 4.55-4.64 (m, 2H, OCH₂Ph); 6.26 (dd, 0.2H, ³J=4.7, ³J=7.4, HC(2) α-anomer); 5.32 (d, 0.8H, ³J=5.6, HC(2) β-anomer); 6.10 (s, 0.8H, HC(1) β-anomer); 6.42 (d, 0.2H, ³J=4.6, HC(1) α-anomer); 7.29-7.36 (m, 5H, Ph); ¹³C-NMR (CDCl₃): 20.55, 20.90, 21.09 (OCO(CH₃)); 58.94 (C(3) α-anomer); 59.98 (C(3) β-anomer); 68.93 (C(5) β-anomer); 69.25 (C(5) α-anomer); 73.50 (OCH₂Ph β-anomer); 73.70 (OCH₂Ph α-anomer); 75.87 (C(2) β-anomer); 81.20 (C(4) β-anomer); 82.75 (C(4) α-anomer); 94.02 (C(1) α-anomer); 98.10 (C(1) β-anomer); 127.56-128.53, 137.72 (Ph); 169.08, 169.62 (OCOCH₃); **FAB-MS**: 290 ([M-OCOCH₃]⁺, 27.8%); 91 ([C₇H₇]⁺, 100%)

3-Azido-5-O-benzyl-1,2-O-bis-(methoxycarbonyl)-3-deoxy-D-ribofuranose (D-9). 305 mg (1.00 mmol) D-7 were deprotected as described for D-8. The yellow oil was dissolved in 4 ml dry CH₂Cl₂, mixed with 770 μl (10.00 mmol) methylchloroformate and cooled to 0°C. 1.12 ml (8.00 mmol) NEt₃ were added dropwise and the mixture was stirred at 0°C for two hours. After addition of 10 ml sat. NaHCO₃-solution and extraction with CH₂Cl₂, the org. fractions were washed with brine, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/EtOAc 4:6) furnished 316 mg (83%) of the anomeric mixture of D-9 as a colorless oil. The anomers were isolated by additional chromatography (PE/TBME 6:4; impregnated onto silica gel from a solution in CH₂Cl₂) and obtained in a ratio of β/α 6.5:1. R_f: α-anomer: 0.26; β-anomer: 0.33 (PE/TBME 6:4); α-anomer: ¹H-NMR (CDCl₃): 3.62 (d, 2H, ³J=2.9, HC(5)); 3.81 (s, 3H, OCOOCH₃); 3.85 (s, 3H, OCOOCH₃); 4.27-4.31 (m, 2H, HC(4), HC(3)); 4.53 (d, 1H, ²J=12.1, OCH_aPh); 4.60 (d, 1H, ²J=12.1, OCH_bPh); 5.17 (dd, 1H, ³J=4.5, ³J=6.7, HC(2)); 6.32 (d, 1H, ³J=4.4, HC(1)); 7.29-7.36 (m, 5H, Ph); ¹³C-NMR (CDCl₃): 55.01, 55.60 (OCOOCH₃); 59.09 (C(3)); 69.08 (C(5)); 73.70 (OCH₂Ph); 74.85 (C(2)); 83.26 (C(4)); 96.82 (C(1)); 127.56-128.53, 137.72 (Ph); 154.35, 154.58 (OCOOCH₃); β-anomer: ¹H-NMR (CDCl₃): 3.68 (d, 2H, ³J=4.1, HC(5)); 3.78 (s, 3H, OCOOCH₃); 3.86 (s, 3H, OCOOCH₃); 4.23-4.35 (m, 2H, HC(4), HC(3)); 4.57 (d, 1H, ²J=12.1, OCH_aPh); 4.62 (d, 1H, ²J=12.1, OCH_bPh); 5.23 (d, 1H, ³J=4.7, HC(2)); 6.08 (s, 1H, HC(1)); 7.31-7.36 (m, 5H, Ph); ¹³C-NMR (CDCl₃): 55.14, 55.60 (OCOOCH₃); 60.14 (C(3)); 68.91 (C(5)); 73.50 (OCH₂Ph); 78.88 (C(2)); 81.46 (C(4)); 100.90 (C(1)); 127.56-128.39, 137.63 (Ph); 153.68, 154.54 (OCOOCH₃); **FAB-MS**: 306 ([M-OCOOCH₃]⁺, 27.2%); 91 ([C₇H₇]⁺, 100%)

2-O-Acetyl-3-azido-5-O-benzyl-1-O-methyl-3-deoxy-D-ribofuranose (D-10). 305 mg (1.00 mmol) D-7 were deprotected as described for D-8. 133 mg (0.50 mmol) of the obtained diol were dissolved in 3 ml MeOH. Two drops of conc. H₂SO₄ were added and the solution was stirred at 4°C for 24 hours. The solution was neutralised with appropriate amounts of Amberlite® IRA-68 resin (*Fluka*), stirred for 20 min. and filtrated. The filtrate was evaporated and purified by chromatography (PE/EtOAc 2:8) (yield 77%). 95 mg (342 µmol) of this 1-O-methylated glycosides were dissolved 4 ml distilled pyridine, mixed with 350 µl (370 µmol) Ac₂O and 8.4 mg (69 µmol) DMAP and stirred at room temperature for 24 hours. After addition of 25 g ice, the mixture was extracted with CH₂Cl₂. The organic fractions were washed with sat. NaHCO₃-solution, dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/EtOAc 8:2) 65.8 mg (60%) of the β-anomer und 17.3 mg (16%) of the α-anomer of D-10 were obtained as colorless oils. R_f: α-anomer: 0.26; β-anomer: 0.38 (PE/EtOAc 6:4); α-anomer: ¹H-NMR (CDCl₃): 2.20 (*s*, 3H, COCH₃); 3.44 (*s*, 3H, C(1)OCH₃); 3.62 (*d*, 2H, ³J=3.5, HC(5)); 4.07-4.13 (*m*, 2H, HC(4), HC(3)); 4.56 (*d*, ²J=12.1, OCH₂Ph); 4.62 (*d*, 1H, ²J=12.1, OCH_bPh); 5.00 (*dd*, 1H, ³J=4.4, ³J=7.2, HC(2)); 5.12 (*d*, 1H, ³J=4.3, HC(1)); 7.26-7.39 (*m*, 5H, Ph); ¹³C-NMR (CDCl₃): 20.49 (COCH₃); 55.44 (OCH₃); 59.32 (C(3)); 69.47 (C(5)); 72.92 (C(2)); 73.66 (OCH₂Ph); 80.54 (C(4)); 101.39 (C(1)); 127.69-128.48 (Ph); 149.80 (OCOCH₃); β-anomer: ¹H-NMR (CDCl₃): 2.15 (*s*, 3H, COCH₃); 3.34 (*s*, 3H, C(1)OCH₃); 3.62 (*d*, 2H, ³J=5.0, HC(5)); 4.07 (*dd*, 2H, ³J=4.8, ³J=7.7, HC(3)); 4.19-4.22 (*m*, 1H, HC(4)); 4.60 (*d*, ²J=12.1, OCH_aPh); 4.63 (*d*, 1H, ²J=12.1, OCH_bPh); 4.87 (*s*, 1H, HC(1)); 5.20 (*d*, 1H, ³J=4.8, HC(2)); 7.28-7.36 (*m*, 5H, Ph); ¹³C-NMR (75 MHz, CDCl₃, TMS): 20.56 (COCH₃); 55.04 (OCH₃); 61.17 (C(3)); 70.70 (C(5)); 73.41 (OCH₂Ph); 76.32 (C(2)); 80.00 (C(4)); 105.96 (C(1)); 127.58-128.35, 137.74 (Ph); 169.78 (OCOCH₃); FAB-MS: 290 ([M-OCH₃]⁺, 21.4%); 91 ([C₇H₇]⁺, 100%)

3-Azido-2-O-benzoyl-5-O-benzyl-1-O-methyl-3-deoxy-D-ribofuranose (D-11). 305 mg (1.00 mmol) D-7 were deprotected as described for D-8. 200 mg (0.75 mmol) of the obtained diol were dissolved in 10 ml MeOH. Two drops of conc. H₂SO₄ were added and the solution was stirred at 4°C for 24 hours. The solution was neutralised with appropriate amounts of Amberlite® IRA-68 resin (*Fluka*), stirred for 20 min. and filtrated. The filtrate was evaporated and purified by chromatography (PE/EtOAc 2:8). The residue was dissolved in 10 ml distilled pyridine, mixed with 105 µl (0.90 mmol) benzoyl chloride und 19 mg (0.16 mmol) DMAP and stirred at room temperature for 2.5 days. After addition of 40 g ice, the mixture was extracted with CH₂Cl₂. The organic fractions were washed with sat. NaHCO₃-solution and water, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/EtOAc 7:3) afforded 260 mg (90%) of the anomeric mixture of D-11 as a colorless oil. R_f: α-anomer: 0.47; β-anomer: 0.56 (PE/EtOAc 8:2); ¹H-NMR (CDCl₃): 3.38 (*s*, 0.8H, OCH₃ β-anomer); 3.44 (*s*, 0.2H, OCH₃ α-anomer); 3.68 (*d*, 2H, ³J=5.0, H₂C(5)); 4.17-4.22 (*m*, 1.2H, HC(4) α-anomer, HC(3) α- and β-anomer); 4.30-4.35 (*m*, 0.8H, HC(4) β-anomer); 4.60-4.65 (*m*, 2H, OCH₂Ph); 5.01 (*s*, 0.8H, HC(1) β-anomer); 5.21 (*dd*, 0.2H, ³J=4.4, ³J=7.7, HC(2) α-anomer); 5.27 (*d*, 0.2H, ³J=4.4, HC(1) α-anomer); 5.44 (*d*, 0.8H, ³J=4.7, HC(2) β-anomer); 7.29-8.12 (*m*, 10H, Ph); ¹³C-NMR (CDCl₃): 55.15 (OCH₃); 58.94 (C(3) α-anomer); 59.67 (C(3) α-anomer); 61.57 (C(3) β-anomer); 70.84 (C(5)); 73.40, 73.52 (OCH₂Ph); 76.74 (C(2)); 80.17 (C(4) β-anomer); 82.51 (C(4) α-anomer); 101.63 (C(1) α-anomer); 106.12 (C(1) β-anomer); 127.64-130.04, 132.86, 133.37, 133.53,

137.79 (Ph); 165.42 (OCOPh); **FAB-MS**: 384 ($[M+H]^+$, 3.3%); 352 ($[M-OCH_3]^+$, 21.5%); 105 ($[C_7H_5O]^+$, 100%); 91 ($[C_7H_7]^+$, 74.2%)

3-Azido-5-O-(4-phenylbenzyl)-3-deoxy-1,2-O-isopropylidene- α -D-ribofuranose (D-12). 112 mg (2.56 mmol) 55-65% NaH was washed three times with pentane and then suspended in 5 ml THF under nitrogen. A solution of 500 mg (2.32 mmol) D-6 in 5 ml THF was added dropwise, then the mixture was stirred at room temperature until the H₂ production has finished. 172 mg (0.46 mmol) TBAI and 470 mg (2.32 mmol) 4-(chloromethyl)biphenyl were added subsequently and the mixture was stirred at room temperature overnight. The solvents were evaporated, the residue was taken up in H₂O and the mixture was extracted with EtOAc. The organic fraction was dried over Na₂SO₄ and evaporated. Chromatographic purification (conditioning in PE/EtOAc 8:2, eluent PE/TBME 6:4) furnished 661 mg (75%) D-12 as a yellowish oil and 108 mg (22%) starting material. R_f: 0.48 (PE/TBME 6:4); ¹H-NMR (CDCl₃): 1.36 (s, 3H, C(CH₃)₂); 1.57 (s, 3H, C(CH₃)₂); 3.63 (dd, 1H, ³J=4.7, ³J=9.6, HC(3)); 3.68 (dd, 1H, ²J_{5a,5b}=11.4, ³J_{5a,4}=3.8, H_aC(5)); 3.84 (dd, 1H, ²J_{5b,5a}=11.4, ³J_{5b,4}=2.5, H_bC(5)); 4.21 (ddd, 1H, ³J_{4,5b}=2.7, ³J_{4,5a}=3.6, ³J_{4,3}=9.6, HC(4)); 4.62 (d, 1H, ²J=12.2, H_AC); 4.68 (d, 1H, ²J=12.2, H_BC); 4.72 (t, 1H, ³J=4.4, HC(2)); 5.83 (d, 1H, ³J=3.6, HC(1)); 7.33 - 7.60 (m, 9H, Ph); ¹³C-NMR (CDCl₃): 26.42 (C(CH₃)₂); 60.53 (C(3)); 67.75 (C(5)); 73.44 (CH₂Ph); 77.90 (C(4)); 79.90 (C(2)); 104.18 (C(1)); 113.06 (C(CH₃)₂); 127.09-128.75(Ph); 136.7, 140.82 (Ph); **FAB-MS**: 381 ($[M]^+$, 2.0%); 167 ($[C_{13}H_{11}]^+$, 100%)

3-Azido-1,2-O-bis-(methoxycarbonyl)-5-O-(4-phenylbenzyl)-3-deoxy-D-ribofuranose (D-13). 300 mg (786 μ mol) D-12 were deprotected in 9.3 ml 75% formic acid as described for D-8. The yellow solid was dissolved in 4.2 ml dry CH₂Cl₂, mixed with 605 μ l (7.86 mmol) methylchloroformate and cooled to 0°C. After adding 877 μ l (6.29 mmol) NEt₃ dropwise, the mixture was stirred at room temperature for two hours. After extraction with sat. NaHCO₃-solution and CH₂Cl₂, the organic fractions were washed with brine, dried over Na₂SO₄ and evaporated. After chromatographic purification (PE/EtOAc 5:5) 356 mg (99%) of the anomeric mixture of D-13 were obtained as a yellowish oil. R_f: 0.55 for α - and β -anomer (PE/EtOAc 6:4); ¹H-NMR (CDCl₃): 3.71 (d, 2H, ³J=4.0, HC(5)); 3.78 (s, 3H, OCOOCH₃); 3.87 (s, 3H, OCOOCH₃); 4.23-4.32 (m, 0.8H, HC(4) β -anomer); 4.33-4.37 (m, 1.2H, HC(3) β -anomer, HC(4), HC(3) α -anomer); 4.61 (d, 1H, ²J=12.1, OCH_aPh); 4.66 (d, 1H, ²J=12.1, OCH_bPh); 5.13 (t, 0.2H, ³J=4.8, HC(2) α -anomer); 5.24 (d, 0.8H, ³J=4.7, HC(2) β -anomer); 6.09 (s, 0.8H, HC(1) β -anomer); 6.34 (d, 0.2H, ³J=4.6, HC(1)); 7.34-7.61 (m, 9H, Ph); ¹³C-NMR (CDCl₃): 55.17, 55.62 (OCOCH₃); 59.80 (C(3) α -anomer); 60.11 (C(3) β -anomer); 68.93 (C(5)); 72.24 (OCH₂Ph β -anomer); 73.54 (OCH₂Ph α -anomer); 78.88 (C(2)); 81.48 (C(4)); 100.90 (C(1) β -anomer); 102.00 (C(1) α -anomer); 127.07-128.75, 136.66, 140.72, 140.82, 137.72 (Ph); 153.68, 154.54 (OCOCH₃); **FAB-MS**: 382 ($[M-OCOCH_3]^+$, 4.1%); 167 ($[C_{13}H_{11}]^+$, 100%).

3-Azido-2-O-benzoyl-1-O-methyl-5-O-(4-phenylbenzyl)-3-deoxy-D-ribofuranose (D-14). 300 mg (786 μ mol) D-12 were dissolved in 11 ml MeOH, mixed with 0.2 ml conc. H₂SO₄ and stirred at 4°C for five days. The solution was neutralised with appropriate amounts of Amberlite® IRA-68 resin (Fluka), stirred for 20 min. and filtrated. The filtrate was evaporated, and the colorless solid was dissolved in 11 ml distilled pyridine. After

addition of 110 μl (943 μmol) benzoyl chloride und 19 mg (156 μmol) DMAP, the mixture was stirred at room temperature overnight. After extraction with $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2$, the organic fractions were washed with sat. NaHCO_3 -solution (3x) and water (1x), dried over Na_2SO_4 and evaporated. Chromatographic purification (PE/EtOAc 8:2) afforded 303 mg (84%) of the anomeric mixture of D-14 as a colorless oil. R_f : α -anomer: 0.37; β -anomer: $R_f=0.45$ (PE/EtOAc 8:2); $^1\text{H-NMR}$ (CDCl_3): 3.40 (s, 0.75H, OCH_3 β -anomer); 3.45 (s, 0.25H, OCH_3 α -anomer); 3.71 (d, 2H, $^3J=5.0$, $\text{H}_2\text{C}(5)$); 4.18-4.24 (m, 1.25H, $\text{HC}(4)$ α -anomer, $\text{HC}(3)$ α - and β -anomer); 4.36 (dt, 0.75H, $^3J=5.0$, $^3J=7.8$, $\text{HC}(4)$ β -anomer); 4.60-4.73 (m, 2H, OCH_2Ph); 5.02 (s, 0.75H, $\text{HC}(1)$ β -anomer); 5.23 (dd, 0.25H, $^3J=4.4$, $^3J=7.1$, $\text{HC}(2)$ α -anomer);); 5.29 (d, 0.25H, $^3J=4.4$, $\text{HC}(1)$ α -anomer); 5.45 (d, 0.75H, $^3J=4.7$, $\text{HC}(2)$ β -anomer); 7.34-8.13 (m, 14H, Ph); $^{13}\text{C-NMR}$ (CDCl_3): 55.20 (OCH_3); 60.36 ($\text{C}(3)$ α -anomer); 61.60 ($\text{C}(3)$ β -anomer); 61.57 ($\text{C}(3)$ β -anomer); 70.92 ($\text{C}(5)$); 73.28 (OCH_2Ph β -anomer); 73.45 (OCH_2Ph α -anomer); 76.78 ($\text{C}(2)$); 80.21 ($\text{C}(4)$ β -anomer); 80.56 ($\text{C}(4)$ α -anomer); 106.18 ($\text{C}(1)$ β -anomer); 127.09-130.07, 133.50, 133.55, 136.85, 140.76, 140.85 (Ph); 165.47 (OCOPh); **FAB-MS**: 428 ($[\text{M}-\text{OCH}_3]^+$, 5.4%); 167 ($[\text{C}_{13}\text{H}_{11}]^+$, 100%); 105 ($[\text{C}_7\text{H}_5\text{O}]^+$, 71.6%).

3-Azido-5-O-(9-fluorenylmethoxycarbonyl)-3-deoxy-1,2-O-isopropylidene- α -D-ribofuranose (D-15). To a solution of 200 mg (0.93 mmol) D-6 in 9.3 ml dist. pyridine were added 288 mg (1.12 mmol) 9-fluorenylmethylchloroformate. After stirring for one hour at room temperature, 5 g ice were added to the yellow solution, and the mixture was extracted three times with CH_2Cl_2 . The organic fractions were washed with sat. NaHCO_3 -solution (1x) and water (2x), dried over Na_2SO_4 and evaporated. After 10 minutes at high vacuum, the product crystallized from the yellow oil. Subsequent crystallization from PE furnished 389 mg (96%) D-15 as a colorless powder. R_f : 0.65 (PE/TBME 6:4); mp: 142-146°C (crystals soften at 136°C); $^1\text{H-NMR}$ (CDCl_3): 1.39 (s, 3H, $\text{C}(\text{CH}_3)_2$); 1.60 (s, 3H, $\text{C}(\text{CH}_3)_2$); 3.47 (dd, 1H, $^3J=4.7$, $^3J=9.6$, $\text{HC}(3)$); 4.24-4.35 (m, 3H, $\text{HC}(4)$, $\text{H}_b\text{C}(5)$, $\text{HC}(9'')$ Fmoc); 4.45 (d, 2H, $^3J=7.2$, H_2C Fmoc); 4.51-4.57 (m, 1H, $\text{H}_a\text{C}(5)$); 4.77 (t, 1H, $^3J=4.3$, $\text{HC}(2)$); 5.84 (d, 1H, $^3J=3.8$, $\text{HC}(1)$); 7.29-7.78 (m, 8H, HC Fmoc); $^{13}\text{C-NMR}$ (CDCl_3): 26.39 ($\text{C}(\text{CH}_3)_2$); 46.69 ($\text{HC}(9'')$ Fmoc), 60.66 ($\text{C}(3)$); 65.44 (H_2C Fmoc); 70.16 ($\text{C}(5)$); 75.56 ($\text{C}(4)$); 79.86 ($\text{C}(2)$); 104.21 ($\text{C}(1)$); 113.35 ($\text{C}(\text{CH}_3)_2$); 120.05, 125.11, 127.16, 127.89, 141.28, 143.19 (Fmoc); 154.88 (OCOO); **FAB-MS**: 437 ($[\text{M}+\text{H}]^+$, 6.5%); 179 ($[\text{dibenzofulvene}]^+$, 100%).

3-Azido-5-O-(9-fluorenylmethoxycarbonyl)-1,2-O-bis-(methoxycarbonyl)-3-deoxy-D-ribofuranose (D-16). 65 mg (149 μmol) D-15 were stirred as a suspension in 1.7 ml 75% formic acid at 60°C for two hours. The solution was evaporated to dryness and then coevaporated twice with 10 ml dioxane and toluene, respectively, and dried at high vacuum. The yellow oil was dissolved in 1.5 ml distilled pyridine, and 114 μl (1.49 mmol) methylchloroformate were added dropwise at 0°C. After stirring at 0°C for one hour. 8 ml H_2O were added and the mixture was extracted three times with CH_2Cl_2 . The organic fractions were washed with sat. NaHCO_3 -solution (2x) and water (2x), dried over Na_2SO_4 and evaporated. Chromatographic purification (PE/EtOAc 8:2, then 6:4) afforded 32.6 mg (43%) of the anomeric mixture of D-16 as a colorless oil. With an additional chromatography, it was possible to isolate the β -anomer, but not pure α -anomer. R_f : α -anomer: 0.39; β -anomer: 0.55 (PE/EtOAc 6:4); β -anomer: $^1\text{H-NMR}$ (CDCl_3): 3.77 (s, 3H, OCOOCH_3);

3.88 (*s*, 3H, OCOOCH₃); 4.24–4.47 (*m*, 7H, H₂C(5), HC(4), HC(3), HC(9'')) Fmoc, H₂C Fmoc); 5.26 (*d*, 1H, ³J=4.4, HC(2)); 6.11 (*s*, 1H, HC(1)); 7.30–7.79 (*m*, 8H, HC Fmoc); ¹³C-NMR (CDCl₃): 46.73 (C(9'')) Fmoc); 55.27, 55.71 (OCH₃); 60.19 (C(3)); 66.31 (CH₂ Fmoc); 70.35 (C(5)); 78.62 (C(2)); 79.82 (C(4)); 100.84 (C(1)); 120.08, 125.20, 127.21, 127.95, 141.32, 143.23, 143.26 (Fmoc); 153.51, 154.51 (OCOCH₃); 154.85 (OCO Fmoc); FAB-MS: 513 ([M]⁺, 4.3%); 438 ([M-OCOCH₃]⁺, 16.3%); 179 ([dibenzofulvene]⁺, 100%)

3'-Azido-6-N-benzoyl-5'-O-benzyl-2'-O-methoxycarbonyl-3'-deoxy-β-D-adenosine (D-17). 117 mg (0.49 mmol) 6-N-Benzoyladenine were suspended in 1.8 ml HMDS and heated to reflux. After addition of some grains of (NH₄)₂SO₄ a clear solution was obtained. After 2 hours at reflux, the solvents were removed at high vacuum at 50°C. The yellow oil was dissolved under argon in 0.75 ml DCE. 144 mg (0.38 mmol) D-9 were dissolved in 8.4 ml CH₃CN and added via syringe. Then, 287 mg (0.45 mmol) TeI₄ were added and the mixture was stirred at reflux for four hours. After cooling to room temperature, 10 ml of sat. NaHCO₃-solution were added, and the mixture was filtered through Celite. The phases were separated and the aqueous phase twice extracted. The organic fractions were washed with water and brine, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/EtOAc 2:8) afforded 77.1 mg (38%) D-17 as a yellowish powder. R_f: 0.30 (PE/EtOAc 2:8); mp: 54–59°C (softens at 38°C); ¹H-NMR (CDCl₃): 3.67–3.72 (*d''d''*, 1H, ²J_{5'a,5'b}=11.0, H_aC(5')); 3.85 (*s*, 3H, OCOOCH₃); 3.85–3.90 (*m*, 1H, H_bC(5')); 4.27–4.29 (*d''t''*, 1H, ³J_{4',3'}=6.0, HC(4')); 4.59 (*d*, 1H, ²J=12.1, OCH_aPh); 4.66 (*d*, 1H, ²J=12.1, OCH_bPh); 4.73 (*dd*, 1H, ³J_{3',4'}=6.0, ³J=5.5, HC(3')); 5.83 (*dd*, 1H, ³J=5.2, ³J=4.1, HC(2')); 6.29 (*d*, 1H, ³J=3.8, HC(1')); 7.29–7.61 (*m*, 8H, Ph); 8.02, 8.04 (2*s*, 2H, Ph); 8.33 (*s*, 1H, HC(8)); 8.78 (*s*, 1H, HC(2)); 9.01 (*br s*, 1H, N⁶HCOPh); ¹³C-NMR (CDCl₃): 55.71 (OCOCH₃); 60.41 (C(3')); 68.34 (C(5')); 73.67 (OCH₂Ph); 78.70 (C(2')); 81.83 (C(4')); 86.73 (C(1')); 123.33 (C(5)); 127.77–128.8, 132.75, 133.46, 136.92 (Ph); 141.49 (C(8)); 149.57 (C(6)); 151.5 (C(4)); 152.82 (C(2)); 154.44 (OCOCH₃); 164.52 (N⁶HCOPh); FAB-MS: 545 ([M+H]⁺, 13.6%); 240 ([benzoyladenine+H]⁺, 19.4%); 91 ([C₇H₇]⁺, 100%).

3'-Azido-6-N,2'-O-dibenzoyl-5'-O-benzyl-3'-deoxy-β-D-adenosine (D-18). 300 mg (0.78 mmol) D-11 and 493 mg (2.06 mmol) 6-N-benzoyladenine were coevaporated twice with 10ml DCE and then suspended in 15ml DCE under argon. After addition of 770 μl (4.12 mmol) MSTFA, the mixture was heated to 60°C until a clear solution was obtained. Then, two portions of 170 μl (0.26 mmol) TMS-OTf each were added via syringe and the mixture was stirred at 60°C overnight. TLC control showed incomplete turnover. Thus, the reaction was allowed to proceed for 24 hours at 80°C. After addition of 35 ml sat. NaHCO₃-solution and 70 ml CH₂Cl₂, the phases are separated and the aqueous phase was extracted twice again. The organic fractions were washed with water, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/EtOAc 2:8) afforded 236.9 mg (51%) D-18 as a yellowish powder. R_f: 0.51 (PE/EtOAc 2:8); mp: 54–61°C (substance softens); ¹H-NMR (CDCl₃): 3.74 (*dd*, 1H, ²J_{5'a,5'b}=10.8, ³J_{5'a,4'}=3.3, H_aC(5')); 3.90 (*dd*, 1H, ²J_{5'b,5'a}=10.8, ³J_{5'b,4'}=2.8, H_bC(5')); 4.36–4.40 (*m*, 1H, HC(4')), 4.62 (*d*, 1H, ²J=12.0, H_aCPh); 4.69 (*d*, 1H, ²J=12.0, H_bCPh); 4.81 (*t*, 1H, ³J=5.5, HC(3')); 6.11 (*dd*, 1H, ³J=5.4, ³J=4.5, HC(2')); 6.45 (*d*, 1H, ³J=4.4, HC(1')); 7.30–7.64 (*m*, 10H, Ph); 8.01–8.09 (*m*, 5H, Ph); 8.38 (*s*, 1H, HC(8)); 8.77 (*s*, 1H, HC(2)); 9.17 (*br s*, 1H, N⁶HCO); ¹³C-NMR (CDCl₃): 61.06 (C(3')); 68.86

(C(5')); 73.79 (OCH₂Ph); 76.40 (C(2')); 82.30 (C(4')); 86.82 (C(1')); 123.31 (C(5)); 127.87-136.98 (Ph); 141.53 (C(8)); 149.65 (C(6)); 151.66 (C(4)); 152.81 (C(2)); 165.42 (N⁶HCOPh); **FAB-MS**: 591 ([M+H]⁺, 12.5%); 352 ([M-(6-N-benzoyladenine)]⁺, 16.4%); 105 ([C₇H₅O]⁺, 100%); **IR** (KBr): 2111cm⁻¹ (N₃).

3'-Azido-6-N-benzoyl-2'-O-methoxycarbonyl-5'-O-(4-phenylbenzyl)-3'-deoxy-adenosine (D-19). 144 mg (0.60 mmol) 6-N-Benzoyladenine and 92 mg (0.20 mmol) D-13 were three times coevaporated in CH₃CN, then suspended in 6 ml CH₃CN under argon and heated to 65°C. After having added 295 μl (1.6 mmol) MSTFA via syringe, there was still a suspension. Thus, eight drops of TMS-OTf were added via syringe, which resulted a clear solution. Subsequently, an additional 45 μl (0.24 mmol) TMS-OTf were added dropwise and the mixture was stirred at 65°C for 23 hours. Although an additional 30 μl TMS-OTf were added after 20 hours, no complete turnover could be achieved. Thus, the mixture was dissolved in each 10 ml sat. NaHCO₃-solution und CH₂Cl₂ and extracted three times. The organic fractions were washed with water, dried over Na₂SO₄ and evaporated. Chromatographic purification (PE/EtOAc 2:8) furnished 58 mg (47%) of the anomeric mixture of D-19 as a yellow powder. R_f: β-anomer: 0.41; α-anomer: 0.34 (PE/EtOAc 2:8); **¹H-NMR** (CDCl₃): 3.64 (s, 3H, C(2')OCOOCH₃); 3.70-3.75 (m, 1H, H_aC(5')); 4.05-4.10 (m, 1H, H_bC(5')); 4.30 (br d, 1H, HC(4')); 4.43-4.50 (m, 1H, HC(3')); 4.69 (d, 1H, ²J=12.2, H_aC(bzl)); 4.83 (d, 1H, ²J=12.2, H_bC(bzl)); 5.15 (t, 0.1H, ³J=4.9, HC(2'), β-anomer); 5.59 (d, 0.9H, ³J=5.0, HC(2') α-anomer); 6.13 (d, 0.1H, ³J=4.7, HC(1') β-anomer); 6.89 (s, 1H, HC(1') α-anomer); 7.33-7.65 (m, 10H, Ph); 8.15-8.32 (m, 4H, Ph); 8.94 (s, 1H, HC(8)); 9.17 (s, 1H, HC(2)); **¹³C-NMR** (CDCl₃): 55.25 (C(2')OCOOCH₃ β-anomer); 55.49 (C(2')OCOOCH₃ α-anomer); 58.22 (HC(3') α-anomer); 58.38 (HC(3') β-anomer); 66.03 (C(5') α-anomer); 66.59 (C(5') β-anomer); 73.40 (OCH₂Ph); 79.88 (C(2') α-anomer); 80.23 (C(2') β-anomer); 81.71, 81.85 (C(4')); 89.74 (C(1') β-anomer); 90.83 (C(1') α-anomer); 114.49 (C(5)); 127.06-141.91 (Ph); 142.93 (HC(8)); 154.14, 154.28 (HC(2), COOCH₃); 175.12 (N⁶HCOPh); **FAB-MS**: 621 ([M+1]⁺, 7.0%); 240 ([6-N-benzoyladenine+H]⁺, 34.5%); 167 ([C₁₃H₁₁]⁺, 100%).

3-Azido-5-O-(methoxycarbonyl)-3-deoxy-1,2-O-isopropylidene-α-D-ribofuranose (D-20). To a solution of 681 mg (3.16 mmol) D-6 in 50 ml pyridine at 0°C were added slowly 1.95 ml (25.28 mmol) methylchloroformate, and the mixture was stirred at room temperature for five hours. After the addition of 100 ml H₂O the mixture was extracted CH₂Cl₂. The organic fractions were washed with sat. NaHCO₃-solution and water, dried over Na₂SO₄ and evaporated. The residue was coevaporated with toluene. 559 mg (88%) of D-20 were obtained as a colorless precipitate. R_f: 0.27 (PE/TBME 6:4); **¹H-NMR** (CDCl₃): 1.37 (s, 3H, CH₃); 1.58 (s, 3H, CH₃); 3.47 (dd, 1H, ³J=9.6, ³J=4.6, HC(3)); 3.81 (s, 3H, OCH₃); 4.23 - 4.31 (m, 2H, HC(4), H_aC(5)); 4.48 - 4.54 (d''d'', 1H, ²J_{5b,5a}=11.8, H_bC(5)); 4.75 (t, 1H, ³J=4.2, HC(2)); 5.82 (d, 1H, ³J=3.6, HC(1)); **¹³C-NMR** (CDCl₃): 26.40 (C(CH₃)₂); 55.09 (OCH₃); 60.54 (C(3)); 65.26 (C(5)); 75.56 (C(4)); 79.87 (C(2)); 104.20 (C(1)); 113.34 (C(CH₃)₂); 155.39 (CH₃OCO); **FAB-MS**: 274 ([M+H]⁺, 21.6%); 216 ([M-CH₃OCO+H]⁺, 74.1%); 43 (100%)

3-Azido-2-O-benzoyl-5-O-(methoxycarbonyl)-1-O-methyl-3-deoxy-β-D-ribofuranose (D-21). 852 mg (3.12 mmol) D-20 in 42 ml MeOH were mixed with 0.7 ml

conc. H_2SO_4 and stirred at 4°C for 6 days. The solution was neutralised with appropriate amounts of Amberlite[®] IRA-68 resin (*Fluka*), stirred for 20 min. and filtrated. The filtrate was evaporated and the residue dissolved in 42 ml pyridine. After addition of 1.3 ml (11.22 mmol) benzoyl chloride and 114 mg (0.94 mmol) DMAP, the solution was stirred at room temperature overnight. 100 ml H_2O were added and the mixture was extracted with CH_2Cl_2 . The organic fractions were washed with sat. NaHCO_3 -solution and water, dried over Na_2SO_4 and evaporated. After chromatographic purification (PE/EtOAc 8:2) 752 mg (69%) of **D-21** were obtained as a colorless oil. R_f : α -anomer: 0.35; β -anomer: 0.43 (PE/EtOAc 8:2); $^1\text{H-NMR}$ (CDCl_3): 3.41 (*s*, 3H, $\text{C}(1)\text{OCH}_3$); 3.83 (*s*, 3H, COOCH_3); 4.21 (*dd*, 1H, $^3J=7.7$, $^3J=4.7$, HC(3)); 4.26-4.35 (*m*, 2H, HC(4), $\text{H}_a\text{C}(5)$); 4.42-4.46 (*d''d''*, 1H, $^2J_{5b,5a}=10.8$, $\text{H}_b\text{C}(5)$); 5.02 (*s*, 1H, HC(1)); 5.46 (*d*, 1H, $^3J=4.7$, HC(2)); 7.44 (*m*, 5H, Ph); $^{13}\text{C-NMR}$ (CDCl_3): 55.11 (OCH_3); 55.25 (OCH_3); 61.27 (C(3)); 67.52 (C(5)); 76.60 (C(2)); 78.71 (C(4)); 106.22 (C(1)); 128.56 (*m*-C Ph); 128.97 (*i*-C Ph); 129.97 (*o*-C Ph); 133.66 (*p*-C Ph); 155.61 (OCOO); 165.40 (COPh); **FAB-MS**: 352 ($[\text{M}+\text{H}]^+$, 11.2%); 320 ($[\text{M}-\text{OCH}_3]^+$, 36.3%); 210 (24.9%); 105 (100%).

9-[3'-Azido-2'-O-benzoyl-5'-O-(methoxycarbonyl)-3'-deoxy- β -D-ribofuranosyl]-6-chloro-9H-purine (D-22). 132 mg (854 μmol) 6-chloropurine were coevaporated twice with DCE and then suspended in 2 ml DCE under argon. After addition of 475 μl (2.56 mmol) MSTFA, the mixture was heated to reflux for 30 min. resulting in a clear, yellow solution. 150 mg (427 μmol) **D-21** were coevaporated twice in DCE, dissolved in 2 ml DCE and added via syringe dropwise in two portions of 1 ml each to the solution of the persilylated base. 235 μl (1.28 mmol) TMS-OTf were added via syringe and the mixture was heated to 80°C overnight. The solution was diluted with 100 ml CH_2Cl_2 , washed with icecold sat. NaHCO_3 -solution, dried over Na_2SO_4 and evaporated. After chromatographic purification (PE/EtOAc 1:1) 117 mg (58%) of **D-22** were obtained as a colorless foam. R_f : 0.47 (PE/EtOAc 1:1); $^1\text{H-NMR}$ (CDCl_3): 3.80 (*s*, 3H, OCH_3); 4.41-4.47 (*m*, 2H, HC(4'), $\text{H}_a\text{C}(5')$); 4.57-4.64 (*d''d''*, 1H, $^2J_{5b,5a}=13.2$, $\text{H}_b\text{C}(5')$); 4.89 (*t*, 1H, $^3J=6.0$, HC(3')); 6.16 (*dd*, 1H, $^3J=3.7$, $^3J=5.6$, HC(2')); 6.36 (*d*, 1H, $^3J=3.7$, HC(1')); 7.46-8.09 (*m*, 5H, Ph); 8.37 (*s*, 1H, HC(8)); 8.78 (*s*, 2H, HC(2)); $^{13}\text{C-NMR}$ (CDCl_3): 55.33 (OCH_3); 60.49 (C(3')); 65.84 (C(5')); 75.80 (C(2')); 80.50 (C(4')); 87.82 (C(1')); 127.98 (C(5)); 128.70 (*m*-C Ph); 130.04 (*i*-C Ph); 132.31 (*p*-C Ph); 134.16 (*p*-C Ph); 143.86 (C(8)); 151.08 (C(6)); 151.62 (C(4)); 152.26 (C(2)); 155.16 (OCOO); 165.36 (PhCO); **FAB-MS**: 474 ($[\text{M}+\text{H}]^+$, 24.0%); 320 ($[\text{M}-\text{base}]^+$, 62.3%); 210 (34.4%); 105 (100%).

3'-Azido-3'-deoxy-D-adenosine (D-23). 200 mg (422 μmol) **D-22** in 2 ml THF were transferred into an autoclave and cooled in liquid nitrogen. NH_3 was condensed into the solution until the mixture was saturated. The autoclave was closed and the mixture was stirred at 60°C overnight. After cooling to room temperature, NH_3 was blown out with nitrogen and the solution evaporated. The residue was submitted to chromatography (EtOAc/MeOH 9:1) which gave 64.1 mg (52%) of **D-23** as a colorless powder. R_f : 0.32 (EtOAc/MeOH/ H_2O 8:1:0.1); mp: 208-212 $^\circ\text{C}$; $[\alpha]_D^{25} = +17.7$ ($c=0.18$, calculated from $\text{OD}=89$, $\epsilon_{260} = 14900 \text{ M}^{-1} \text{ cm}^{-1}$; MeOH); $^1\text{H-NMR}$ (CD_3OD): 3.74 (*dd*, 1H, $^2J_{5a,5b}=12.6$, $^3J_{5a,4}=2.7$, $\text{H}_a\text{C}(5')$); 3.88 (*dd*, 1H, $^2J_{5b,5a}=12.6$, $^3J_{5b,4}=2.5$, $\text{H}_b\text{C}(5')$); 4.13 (*d''d''*, 1H, $^3J=3.0$, HC(4')); 4.31 (*dd*, 1H, $^3J=3.2$, $^3J=5.6$, HC(3')); 5.07 (*t*, 1H, $^3J=5.9$, HC(2')); 5.95 (*d*, 1H, $^3J=6.3$, HC(1')); 8.18,

(*s*, 1H, HC(2)); 8.31 (*s*, 1H, HC(8)); $^{13}\text{C-NMR}$ (CD_3OD): 63.47 (C(5')); 64.07 (C(3')); 76.09 (C(2')), 85.44 (C(4')); 91.02 (C(1')); 121.06 (C(5)); 141.96 (C(8)); 150.03 (C(4)); 153.62 (C(2)); 157.63 (C(6)); **FAB-MS**: 293 ($[\text{M}+\text{H}]^+$, 19.4%); 71 (100%); **IR** (KBr): 2114 cm^{-1} (N_3).

3'-Amino-3'-deoxy-D-adenosine (D-24). A suspension of 54 mg (185 μmol) D-23 and a catalytic amount of Pd/C in 8 ml ethanol was hydrated under normal pressure for 6 hours. The catalyst was filtered through Celite and washed with 100 ml $\text{H}_2\text{O}/\text{MeOH}$ (1:1). The filtrate was evaporated, lyophilised and dried over P_2O_5 at high vacuum, resulting in 70.4 mg (97%) D-24 as a colorless powder. R_f : 0.07 ($\text{EtOAc}/\text{MeOH}/\text{H}_2\text{O}$ 4:1:0.3); mp: $>230^\circ\text{C}$; $[\alpha]_D^{25} = -15.9$ ($c=0.19$, calculated from $\text{OD}=106$, $\epsilon_{260}=14900 \text{ M}^{-1} \text{ cm}^{-1}$; H_2O) $^1\text{H-NMR}$ (DMSO-d_6): 1.78 (*br s*, 2H, N^3H_2); 3.54 (*t*, 1H, $^3\text{J}=6.0$, HC(3')); 3.67 (*dd*, 1H, $^2\text{J}=12.5$, $^3\text{J}=3.6$, $\text{H}_a\text{C}(5')$); 3.80 (*dd*, 1H, $^2\text{J}=12.5$, $^3\text{J}=1.9$, $\text{H}_b\text{C}(5')$); 3.90 (*m*, 1H, HC(4')); 4.28 (*dd*, 1H, $^3\text{J}=2.8$, $^3\text{J}=5.3$, HC(2')); 5.90 (*d*, 1H, $^3\text{J}=2.8$, HC(1')); 7.26 (*br s*, 2H, N^6H_2); 8.13, 8.37 (2*s*, 2H, HC(2), HC(8)); $^{13}\text{C-NMR}$ (DMSO-d_6): 52.61 (C(3')); 61.09 (C(5')); 74.8 (C(2')); 85.60 (C(4')); 89.18 (C(1')); 119.17 (C(5)); 139.37 (C(8)); 148.87 (C(4)); 152.50 (C(2)); 156.09 (C(6)); **FAB-MS** (glycerol): 267 ($[\text{M}+\text{H}]^+$, 85.1%); 136 ($[\text{base}+\text{H}]^+$, 100%)

1-O-Acetyl-3-azido-2-O-benzoyl-5-O-methoxycarbonyl-L-ribofuranose (L-25). 6.43 g (18.30 mmol) L-21 were dissolved in 10.34 ml Ac_2O and 4.59 ml AcOH . The mixture was cooled to 0°C and 1.47 ml H_2SO_4 were added dropwise. After stirring 10 min at 0°C , the mixture was left overnight at 4°C in the fridge. After adding 250 g of ice, the mixture was stirred for 2 hours, then extracted with CH_2Cl_2 (3 x 500 ml). The organic phase was washed with sat. NaHCO_3 -solution (4 x 250 ml), dried over Na_2SO_4 and evaporated. Purification by chromatography (PE/EE 9:1) afforded 2.42 g (37%) of the α -anomer and 3.73 g (57%) of the β -anomer of L-25 as yellow oils. R_f : α -anomer: 0.25; β -anomer: 0.32 (PE/ EtOAc 8:2); $^1\text{H-NMR}$ (CDCl_3): β -anomer: 2.12 (*s*, 3H, CH_3COO); 3.83 (*s*, 3H, CH_3OCO); 4.28–4.51 (*m*, 4H, HC(3), HC(4), $\text{H}_2\text{C}(5)$); 5.58 (*d*, 1H, $^3\text{J}=3.9$, HC(2)); 6.28 (*s*, 1H, HC(1)); 7.45–8.08 (*m*, 5H, Ph). α -anomer: 2.16 (*s*, 3H, CH_3COO); 3.76 (*s*, 3H, CH_3OCO); 4.22 (*dd*, 1H, $^3\text{J}=8.0$, 4.8, HC(3)); 4.30 (*dd*, 1H, $^2\text{J}_{5a,5b}=12.3$, $^3\text{J}_{5a,4}=2.8$, $\text{H}_a\text{C}(5)$); 4.55 (*dd*, 1H, $^2\text{J}_{5b,5a}=12.3$, $^3\text{J}_{5b,4}=4.7$, $\text{H}_b\text{C}(5)$); 5.18 (*ddd*, 1H, $^3\text{J}_{4,5a}=2.8$, $^3\text{J}_{4,5b}=4.7$, $^3\text{J}=7.7$, HC(4)); 5.64 (*t*, 1H, $^3\text{J}=4.9$, HC(2)); 7.22 (*d*, 1H, $^3\text{J}=5.1$, HC(1)); 7.48–8.07 (*m*, 5H, Ph); $^{13}\text{C-NMR}$ (CDCl_3): β -anomer: 20.89 (CH_3CO); 55.14 (CH_3OCO); 60.33 (C(3)); 66.04 (C(5)); 76.01 (C(2)); 79.61 (C(4)); 98.04 (C(1)); 128.62, 129.95, 130.02, 133.84 (Ph); 155.46 (COOCH_3); 165.19 (PhCO); 168.85 (CH_3CO); α -anomer: 20.42 (CH_3CO); 54.97 (CH_3OCO); 60.64 (C(3)); 69.99 (C(5)); 70.70 (C(2)); 79.54 (C(4)); 86.34 (C(1)); 128.60, 129.56, 129.92, 133.75 (Ph); 155.22 (COOCH_3); 164.75 (PhCO); 169.54 (CH_3CO). **FAB-MS**: 418 ($[\text{M}+\text{K}]^+$, 23.7%); 320 ($[\text{M}-\text{COCH}_3]^+$, 41.4%); 105 (100%)

9-[3'-Azido-2'-O-benzoyl-5'-O-(methoxycarbonyl)-3'-deoxy- β -L-ribofuranosyl]-6-chlor-9H-purine (L-22). 188 mg (0.50 mmol) L-25 (pure β -anomer) and 153 mg (0.99 mmol) 6-chloropurine were coevaporated three times with DCE under argon. 5 ml DCE and 0.46 ml (2.48 mmol) MSTFA were added. The mixture was stirred at 60°C until the base was completely solubilised. 135 μl (0.74 mmol) TMS-OTf were added, the temperature was allowed to reach 75°C and the mixture was stirred overnight. 40 ml CH_2Cl_2 were

added and the organic phase was washed with sat. NaHCO_3 -solution. After drying over Na_2SO_4 and evaporation, purification by chromatography (PE/EtOAc 8:2, then 5:5) furnished 190 mg (81%) L-22 as a white foam. R_f : 0.54 (PE/EtOAc 5:5); $^1\text{H-NMR}$ (CDCl_3): 3.80 (*s*, 3H, CH_3OCO); 4.42–4.47 (*m*, 2H, $\text{HC}(4')$, $\text{H}_a\text{C}(5')$); 4.58–4.64 (*m*, 1H, $\text{H}_b\text{C}(5')$); 4.90 (*t*, 1H, $^3J=6.0$, $\text{HC}(3')$); 6.16 (*dd*, 1H, $^3J=5.7$, $^3J=3.6$, $\text{HC}(2')$); 6.37 (*d*, 1H, $^3J=3.6$, $\text{HC}(1')$); 7.48–8.08 (*m*, 5H, Ph); 8.38 (*s*, 1H, $\text{HC}(8)$), 8.78 (*s*, 1H, $\text{HC}(2)$); $^{13}\text{C-NMR}$ (CDCl_3): 55.33 (CH_3OCO); 60.52 ($\text{C}(3')$); 65.86 ($\text{C}(5')$); 75.80 ($\text{C}(2')$); 80.51 ($\text{C}(4')$); 87.84 ($\text{C}(1')$); 128.01 ($\text{C}(5)$); 128.71, 130.04, 132.32, 134.16 (Ph); 143.90 ($\text{C}(8)$); 151.09 ($\text{C}(6)$); 151.61 ($\text{C}(4)$); 152.26 ($\text{C}(2)$); 155.17 (COOCH_3); 165.36 (PhCO); **FAB-MS**: 474 ($[\text{M}+\text{H}]^+$, 19.3%); 320 ($[\text{M-base}]^+$, 44.7%); 105 (100%)

3'-Azido-3'-deoxy-L-adenosine (L-23). 1.950 g (3.75 mmol) L-22 was dissolved in 100 ml MeOH in an autoclave and cooled to -78°C . NH_3 gas (50 ml) was condensed into the mixture at -78°C . The mixture was allowed to reach room temperature and then was heated to 60°C overnight. After cooling to 0°C , the mixture was evaporated and purified by chromatography (EtOAc/MeOH 9:1) to give 799 mg (73%) of L-23 as a white solid. R_f : 0.38 (EtOAc/MeOH/ H_2O 8:1:0.1); mp: decomposition at $191\text{--}195^\circ\text{C}$; $[\alpha]_D^{25} = -17.6$ ($c=2.3$, calculated from $\text{OD}=116$, $\epsilon_{260}=14900 \text{ M}^{-1} \text{ cm}^{-1}$; MeOH); $^1\text{H-NMR}$ (DMSO-d_6 , 400 MHz): 3.54–3.72 (*m*, 2H, $\text{H}_2\text{C}(5')$); 3.99 (*q*, 1H, $^3J=3.5$, $\text{HC}(4')$); 4.32 (*dd*, 1H, $^3J=5.5$, $^3J=3.5$, $\text{HC}(3')$); 5.01 (*q*, 1H, $^3J=5.8$, $\text{HC}(2')$); 5.64 (*dd*, 1H, $^3J=7.4$, $^3J=4.4$, $\text{HO-C}(5')$); 5.90 (*d*, 1H, $^3J=6.2$, $\text{HC}(1')$); 6.26 (*d*, 1H, $^3J=5.5$, $\text{HO-C}(2')$); 8.15 (*s*, 1H, $\text{HC}(2)$); 8.36 (*s*, 1H, $\text{HC}(8)$); $^{13}\text{C-NMR}$ (DMSO-d_6 , 100 MHz): 61.63 ($\text{C}(5')$); 62.15 ($\text{C}(3')$); 73.91 ($\text{C}(2')$); 82.93 ($\text{C}(4')$); 87.98 ($\text{C}(1')$); 119.38 ($\text{C}(5)$); 139.98 ($\text{C}(8)$); 148.98 ($\text{C}(4)$); 152.51 ($\text{C}(2)$); 156.24 ($\text{C}(6)$); **FAB-MS**: 293 ($[\text{M}+\text{H}]^+$, 100%); 136 ($[\text{base}+\text{H}]^+$, 93.3%); **IR** (KBr): 2108 cm^{-1} (N_3).

3'-Amino-3'-deoxy-L-adenosine (L-24). A suspension of 60 mg (205 μmol) L-23 and a catalytic amount of Pd/C in 4 ml ethanol was hydrated under normal pressure overnight. The catalyst was filtered through Celite and washed with 100 ml $\text{H}_2\text{O}/\text{MeOH}$ (1:1). The filtrate was evaporated, lyophilised and dried over P_2O_5 at high vacuum, resulting in 36 mg (67%) L-24 as a colorless powder. R_f : 0.07 (EtOAc/MeOH/ H_2O 4:1:0.3); mp: decomposition at 230°C ; $[\alpha]_D^{25} = +16.8$ ($c=0.06$, calculated from $\text{OD}=35$, $\epsilon_{260}=14900 \text{ M}^{-1} \text{ cm}^{-1}$; H_2O); ^1H -, ^{13}C -NMR and MS data as for D-24.

Acknowledgement: We thank Dr. S. Gunzenhauser for valuable technical assistance and the Swiss National Science Foundation for the financial support.

References

- [1] Suhadolnik RJ. Nucleoside Antibiotics. New York: Wiley-Interscience, 1970.
- [2] Suhadolnik RJ. Nucleosides as Biological Probes. New York: Wiley-Interscience, 1979.
- [3] Baker BR, Joseph JP, Williams JH. *J. Am. Chem. Soc.* **1955**, *77*, 1.
- [4] Herdewijn P, Balzarini J, Masanori B, Pauwels R, Van Aerschot A, Janssen G, De Clercq E. *J. Med. Chem.* **1988**, *31*, 2040-2048 and references therein.
- [5] Nolte A, Klußmann S, Bald R, Erdmann VA, Fürste JP. *Nature Biotechnology* **1996**, *14*, 1116-1119.
- [6] Mengel R, Wiedner H. *Chem. Ber.* **1976**, *109*, 433-443.
- [7] Samano MC, Robins MJ. *Tetrahedron Lett.* **1989**, *30*, 2329-2332.
- [8] Robins MJ, Hawrelak SD, Hernández AE, Wnuk SF. *Nucleosides & Nucleotides* **1992**, *11*, 821-834.
- [9] García-Alles LF, Magdalena J, Gotor V. *J. Org. Chem.* **1996**, *61*, 6980-6986.
- [10] Robins MJ, Zou R, Hansske F, Wnuk SF. *Can. J. Chem.* **1997**, *75*, 762-767.
- [11] Baker BR, Schaub RE, Kissman HM. *J. Am. Chem. Soc.* **1955**, *77*, 5911-5915.
- [12] Wofrom ML, Winkley MW. *J. Org. Chem.* **1967**, *32*, 1823-1825.
- [13] Hobbs JB, Eckstein F. *J. Org. Chem.* **1977**, *42*, 714-719.
- [14] Azhaye AV, Smrt J. *Collect. Czech. Chem. Commun.* **1978**, *43*, 1520-1530.
- [15] Azhaye AV, Ozols AM, Bushnev AS, Dyatkina NB, Kochetova SV, Victorova LS, Kukhanova MK, Krayevsky AA, Gottokh BP. *Nucleic Acids Res.* **1979**, *6*, 625-643.
- [16] Imazawa M, Eckstein F. *J. Org. Chem.* **1979**, *44*, 2039-2041.
- [17] Soenens J, François, Van den Eeckhout E, Herdewijn P. *Nucleosides & Nucleotides* **1995**, *14*, 409-411.
- [18] Beigelman L, Karpeisky A, Matulic-Adamic J, Haeberli P, Sweedler D, Usman N. *Nucleic Acids Res.* **1995**, *23*, 4434-4442.
- [19] Vorbrüggen H, Krolkiewicz K, Bennua B. *Chem. Ber.* **1981**, *114*, 1234-1255.
- [20] Ibrahim ES, Elgemeie GEH, Abbasi MM, Abbas YA, Eldbadawi MA, Attia AME. *Nucleosides & Nucleotides* **1995**, *14*, 1425-1423.
- [21] Frame AS, Wightman RH, Mackenzie G. *Tetrahedron* **1996**, *52*, 9219-9236.
- [22] Jungmann O, Pfeleiderer W. *Tetrahedron Lett.* **1996**, *37*, 8355-8358.
- [23] Seela F, Zulauf M. *Synthesis* **1996**, 726-730.
- [24] Martin, P. *Helv. Chim. Acta* **1996**, *79*, 1930-1938.
- [25] Van Straten NCR, van der Marel GA, van Boom JH. *Tetrahedron* **1997**, *53*, 6509-6522.
- [26] Knapp S. *Chem. Rev.* **1995**, *95*, 1859-1876.
- [27] Poopeiko NE, Kvasyuk EI, Mikhailopulo IA, Lidaks MJ. *Synthesis* **1985**, 605-609.
- [28] Ozols AM, Azhaye AV, Dyatkina NB, Krayevsky AA. *Synthesis* **1980**, 557-559.
- [29] Vorbrüggen H, Höfle G. *Chem. Ber.* **1981**, *114*, 1256-1268.
- [30] Recondo EF, Rinderknecht H. *Helv. Chim. Acta* **1959**, *42*, 1171-1173.
- [31] Shimomura N, Matsutani T, Mukaiyama T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3100-3106.
- [32] Czech BP, Bartsch RA. *J. Org. Chem.* **1984**, *49*, 4076-4078.
- [33] Bolitt V, Mioskowski C. *J. Am. Chem. Soc.* **1991**, *113*, 6320-6321.
- [34] Gioeli C, Chattopadhyaya JB. *J. Chem. Soc., Chem. Commun.* **1982**, 672-674.
- [35] Ueki M, Amemiya M. *Tetrahedron Lett.* **1987**, *28*, 6617-6620.
- [36] Nagai M, Matsutani T, Mukaiyama T. *Heterocycles* **1996**, *42*, 57-63.
- [37] P. Martin, *Helv. Chim. Acta* **1995**, *78*, 486-504.
- [38] Seela F, Zulauf M, Rosemeyer H, Reuter H. *J. Chem. Soc., Perkin Trans. 2* **1996**, 373-2376.
- [39] E. Moyroud, unpublished results.