Synthesis of Purine and Pyrimidine 3′-Amino-3′-deoxy- and 3′-Amino-2′,3′-dideoxyxylonucleosides

Luis F. García-Alles, Julia Magdalena, and Vicente Gotor*

Departamento de Química Orgánica e Inorgánica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

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A general procedure to obtain the 3′-aminoxylonucleosides **13a**,**b** and **17a**,**b** is presented. The synthetic scheme is based on the 5′ directed intramolecular nucleophilic substitution at the 3′-activated position of the nucleoside. The approach of the incoming group to this position takes place regio- and stereoselectively from the most hindered face of the nucleoside. The methodology presented is applicable to ribonucleosides and 2′-deoxyribonucleosides, regardless of their nitrogenated base.

Introduction

Polyoxin and puromycin are important examples of compounds which can be classified as aminosugar nucleosides. These and some other derivatives are known to possess strong antibacterial, anticancer, and biosynthetic inhibitory properties.[1]

Considerable effort has been devoted to the preparation of this kind of compounds. Generally, the most successful procedures have been those describing their synthesis *via* reduction of the sugar-substituted azido analogs.[2] Some other approaches have also been reported.[3] Among them, two successful strategies took advantage of the presence of a neighboring hydroxyl group to deliver intramolecularly the amine nucleophile to the new position.[3c,d]

However, all of these procedures are strongly dependent on the nature of the nitrogenated base present in the starting nucleoside. An illustrating example can be the work reported by Matsuda *et al.*, where treatment of an analog of 3′-*O*-mesylthymidine with NaN_3 gave rise to a mixture of several compounds coming from intervention of the base in different ways.[4]

The objective is even more complicated when one wishes to obtain a 3′-aminoxylonucleoside. In this case the nucleophile must approach the 3′-position from the most hindered side of the nucleoside: the β-face. While for purine nucleosides, attacks from this face are still possible, pyrimidine nucleosides usually resist such transformation, since the incoming nucleophile must compete with the favorable intramolecular attack of the 2-carbonyl group of the pyrimidine base.[5] For ribonucleosides, an added complication is found since both the 3′- and the 2′-positions are capable of undergoing substitution. Despite the fact that the 3′- position is generally the most reactive one, in most of the reported cases small amounts of the 2′-substituted products were also found.[2e,g]

It would be important, from our point of view, to develop a general methodology which could be applied to obtain 3′-amino-3′-deoxy- and 3′-amino-2′,3′-dideoxyxylonucleosides. There are two main features of the procedure we describe in this paper. (1) It has been extended to ribonucleosides and 2′-deoxyribonucleosides, containing both purine and pyrimidine bases in their structures. (2) The amino substitution is delivered to the 3′-position from the most hindered face of the nucleoside with total regio- and stereoselectivity.

Results and Discussion

Synthesis of 3′-Amino-2′,3′-dideoxyxylonucleosides 13 a,b. The synthetic strategy we have developed is based on the introduction of the amino function at the 3′-position from the neighboring 5′-position of the sugar skeleton of the nucleoside.[6] To achieve this goal, we functionalized the 5′-position with a group able to release the amino function at the 3′-position: the carbamoyl group had been previously used with a similar purpose.[3c,7] On the other hand, it was also necessary to activate the 3′-position for nucleophilic substitution to take place. Bearing all this in mind, the first step was to obtain compounds **4**−**8** (see Scheme 1).

Candida antarctica lipase (CAL) was used as the synthetic tool which permits one to obtain carbonates **2** and **3** from the starting 2′-deoxyribonucleosides **1** (B = Th, Ad) with high regioselectivity. The potential power of this and other enzymes in nucleoside chemistry had been previously studied in our group.[8] We have used acetone *O*-[(phenyloxy)carbonyl]oxime for thymidine **1**, since the regioselectivity of the process is better than that

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(3) (a) Miller, N.; Fox, J. J. *J. Org. Chem.* **1964**, *29*, 1772. (b) Mitsunobu, O.; Takizawa, S.; Morimato, H. *J. Am. Chem. Soc.* **1976**, *98*, 7858. (c) Samano, M. C.; Robins, M. J. *Tetrahedron Lett.* **1989**, *30*, 2329. (d) McGee, D. P. C.; Sebesta, D. P.; O'Rourke, S. S.; Martínez, R. L.; Jung, M. E.; Piecken, W. A. *Tetrahedron Lett.* **1996**, *37*, 1995.

(4) Matsuda, A.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1980**, *45*, 3274.

(5) Many syntheses of 3′- (or 2′-) amino ribonucleosides have been reported to proceed *via* the 2,3′-(or the 2,2′-)anhydronucleosides.[2c,d,3a,d]

(6) This kind of methodology had been previously used to invert configuration at the 3′-position of purine nucleosides: Herdewijn, P. A. M. *J. Org. Chem.* **1988**, *53*, 5050.

(7) (a) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109. (b) Roush, W. R.; Adam, M. A. *J. Org. Chem.* **1985**, *50*, 3752.

(8) (a) Morís, F.; Gotor, V. *J. Org. Chem.* **1992**, *57*, 2490. (b) Morís, F.; Gotor, V. *Tetrahedron* **1992**, *48*, 9869. (c) García-Alles, L. F.; Gotor, V. *Tetrahedron* **1995**, *51*, 307.

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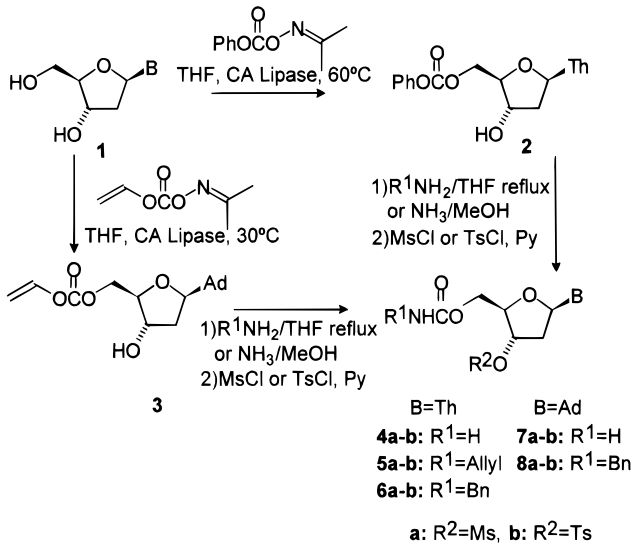
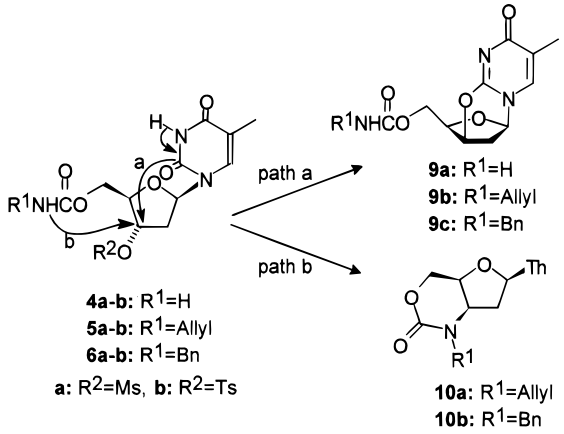
Scheme 1



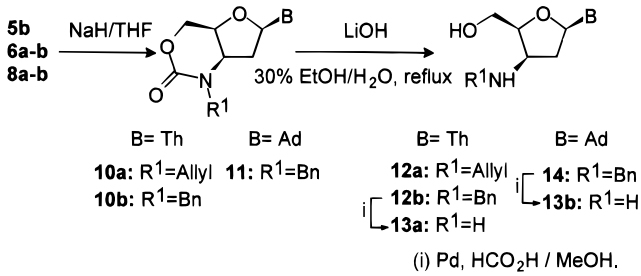
Scheme 2



obtained using the vinyl carbonate, and in consequence the final yield of **2** is increased. Treatment of **2** or **3** with the corresponding amine yields the 5′-carbamate,[8c] and finally, reaction with mesyl or tosyl chloride gave the 3′-activated compounds **4a,b**, **5a,b**, and **6a,b** for thymidine (Th) and **7a,b** and **8a,b** for adenosine (Ad).

As previously mentioned, it is well-known that introduction of nucleophiles at the 3′-activated position of pyrimidine nucleosides is difficult to perform, since the main product usually results to be the 2, 3′-anhydronucleoside. For this reason, we studied the conditions which would favor formation of products **10** (through path b in Scheme 2) over formation of the 2,3′-anhydro derivatives **9**. From the very beginning it seemed clear that using basic aqueous media the 2,3′-anhydro derivative was always obtained as the main product of reaction, regardless of the R^1 and R^2 groups present in the starting material. This was in complete agreement with other reported results.[9] However, we found that product **10** could be obtained when NaH in anhydrous THF was used as the proton abstraction system,[3c,7b] and both the R^1 and R^2 groups were adequately selected. Thus, whereas **9a** was the only product obtained from **4a,b** (R^1 = H), **6a,b** (R^1 = Bn) yielded almost quantitatively **10b**. Small amounts of product **9c** were also isolated from the

Scheme 3



reaction with **6a** (when R^2 = Ms). An intermediate situation was found when **5a,b** (R^1 = allyl) were used. In this case, the pathway followed depends dramatically on the R^2 group, resulting almost exclusively **9b** from **5a** (path a in Scheme 2) and **10a** from **5b** (path b). The reasons for this behavior have not been studied in detail at this point.

Once we knew the optimum conditions to perform the key step of the synthetic strategy, we completed the synthesis of the 3′-amino-3′-deoxyxylothymidine **13a** as follows (see Scheme 3). Carbamates **10a,b** were decarbonylated with LiOH, yielding 3′-*N*-allyl- and 3′-*N*-benzylamino-3′-deoxyxylothymidine **12a,b**. Finally, **13a** was quantitatively formed when **12b** was submitted to catalytic transfer hydrogenation, using formic acid in presence of palladium black.[10] This amino nucleoside was also obtained from **12a** using $(PPh_3)_3RhCl$,[11] but with poorer results (longer reaction time and approximately 60% yield by TLC). Data for product **13a,** obtained following this synthetic scheme, was shown to be in complete accord with data reported by Matsuda *et al.* for the compound synthesized following an alternative strategy.[4]

As far as the synthesis of the adenosine derivative **13b** is concerned, the intramolecular displacement step at the 3′-position does not present the aforementioned problem of the pyrimidine nucleosides. When **7a,b** (R^1 = H) were submitted to reaction (NaH/THF), the expected amino sugar nucleoside was not obtained. However, the 5′-*O*-(*N*-benzylcarbamoyl)-3′-*O*-methylsulfonyl-2′-deoxyadenosine derivative **8a** yielded **11** with good yield (Scheme 3), together with a small amount of a second unknown product (<10%). Formation of this undesired product was avoided using the tosyl derivative **8b**, showing once again the suitability of this leaving group. The synthetic scheme was then completed from **11** to give **13b**.[2h]

The identification of the 3′-amino xylonucleoside derivatives was accomplished by ^{13}C-NMR spectroscopy. The main difference was a *ca.* 15−20 ppm upfield shift of the peak corresponding to the 3′-carbon atom with regard to the starting 2′-deoxyribonucleosides. Complete ^{1}H- and ^{13}C-NMR spectral data are given in Tables 1 and 2, respectively.

On the other hand, the stereochemistry of the sugar ring was confirmed by means of NOE difference experiments performed on the rigid cyclic carbamates **10b** and **11**. As can be seen in Table 3 (see also Chart 1), 3.2−5.6% and 5.0−9.2% enhancements of the H3′ signal were observed when the H4′ and H2′α signals of **10b** and **11** were irradiated. This is a clear indication of the relative disposition of these hydrogen atoms toward the same side of the sugar framework.

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(11) Laguzza, B. C.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 1483.

Table 1. ^{1}H-NMR Spectral Data (only noninterchangable signals)[a] in δ (ppm)

	base ring			sugar moiety						
product	H6(H2)	H5(H8)	Me	H1′	H2′α	H2′β	H3′	H4′	H5′(2 H)	other
10a	7.25 (s)		1.88 (s)	6.08 (t)	2.73 (m)	2.06 (m)	4.12 (m)	4.50 (m)	4.41−4.19 (m)	5.73 (m), 5.2−5.3 (2H,m), 4.14 (m), 3.6 (m)
10b	7.25 (s)		1.90 (s)	6.03 (t)	2.54 (m)	1.95 (m)	3.99 (m)	4.39 (m)	4.45−4.21 (m)	7.31 (5H, m), 4.86 (d), 4.16 (d)
11	8.21 (s)	8.27 (s)		6.35 (dd)	2.85 (m)	3.02 (m)	4.28 (m)	4.67 (m)	4.45 (m)	7.35 (5H, m), 4.86 (d), 4.32 (d)
12a	8.20 (s)		2.07 (s)	6.30 (t)	2.83 (m)	2.35 (m)	3.65 (m)	4.35 (m)	4.15 (m)	6.15 (m), 5.6−5.4 (2H, m), 4.02 (m), 3.55 (m)
12b	8.35 (s)		2.05 (s)	6.29 (t)	2.72 (m)	2.23 (m)	3.79 (m)	4.30 (m)	4.12 (m)	7.50 (5H, m), 3.95 (2H, m)
14	8.22 (s)	8.57 (s)		6.30 (t)	2.71 (m)	2.55 (m)	3.65 (m)	4.17 (m)	3.88 (m)	7.45 (5H, m), 3.85 (2H, m)
13b[2h]	7.80 (s)	7.89 (s)		6.02 (dd)	2.32 (m)	2.90 (m)	3.97 (m)	4.12 (m)	3.87 (m)	
22	7.41 (d)	6.21 (d)		6.58 (d)	5.54 (d)		4.73 (m)	4.62 (m)	4.23 (m)	7.45 (5H, m), 4.40 (2H, m)
24	8.31 (s)	8.48 (s)		6.40 (s)		4.65 (d)	4.43 (d)	4.48 (m)	4.50−4.12 (m)	7.35 (5H, m), 4.25 (2H, m)
25a	7.66 (d)	5.80 (d)		5.73 (d)		4.39 (m)	3.97 (dd)	4.78 (m)	4.45 (m)	7.44 (5H, m), 4.83 (d), 4.50 (d)
25b	8.22 (s)	8.32 (s)		5.94 (d)		5.11 (m)	4.04 (dd)	4.83 (m)	4.45 (m)	7.43 (5H, m), 4.91 (d), 4.40 (d)
26a	8.33 (d)	5.90 (d)		6.01 (d)		4.57 (dd)	3.69 (dd)	4.51 (m)	4.08 (m)	7.46 (5H, m), 4.15 (2H, m)
26b	8.25 (s)	8.55 (s)		5.91 (d)		4.76 (dd)	3.49 (dd)	4.35 (m)	3.85 (m)	7.45 (5H, m), 4.00 (2H, m)
17a	7.74 (d)	5.79 (d)		5.60 (d)		4.65 (dd)	3.92 (dd)	4.35 (m)	3.95−3.75 (m)	
17b[2e]	7.66 (s)	7.91 (s)		5.59 (d)		4.52 (dd)	3.68 (dd)	4.27 (m)	3.77 (m)	

[a] Solvents: DMSO-d_6, except for **10a** and **10b** ($CDCl_3$), **12a**, **12b**, **22**, and **26a** (CD_3OD), and **13b**, **17a**, and **17b** (D_2O). ^{1}H-NMR signals of the sugar moiety were assigned using selective homodecoupling experiments.

Table 2. ^{13}C-NMR Chemical Shifts[a] in δ (ppm)

	base ring					sugar moiety					
product	C2	C4	C5	C6	Me/C8	C1′	C2′	C3′	C4′	C5′	other
10a	150.34	163.87	111.18	133.98	12.21	83.79	38.19	56.03	74.60	65.96	153.37, 131.80, 118.99, 49.53
10b	150.30	163.81	111.41	133.86	12.37	83.69	38.09	55.73	74.62	66.18	154.15, 135.49, 128.71, 128.18, 127.99, 50.36
11	153.08	149.53	119.64	156.48	138.56	83.81	36.75	57.04	74.60	65.72	153.92, 137.35, 128.90, 128.09, 127.70, 49.97
12a	152.67	166.51	111.98	139.99	12.76	86.84	35.84	59.25	80.43	61.49	132.24, 122.12, 50.91
12b	152.94	167.00	111.52	139.66	13.08	85.77	39.28	59.53	83.23	62.81	141.56, 129.99, 129.84, 128.69, 53.75
14	152.47	148.90	119.32	156.28	140.69	82.93	37.46	57.94	81.83	61.16	140.17, 128.30, 128.09, 126.80, 51.73
13a	150.79	164.13	110.15	137.08	12.40	83.08	35.67	50.38	78.24	59.29	
13b	152.27	147.40	119.39	155.57	142.05	84.36	36.97	51.92	80.19	60.04	
22	162.85	176.24	110.85	139.66		93.00	91.87	77.30	89.09	65.75	158.64, 141.10, 130.33, 129.06, 129.00, 46.27
24	152.91	149.14	119.03	156.20	139.58	82.37	57.58	58.30	78.31	63.66	156.05, 139.94, 128.32, 127.07, 126.85, 43.88
25a	150.56	163.26	102.14	139.74		89.59	77.83	63.43	72.94	65.99	153.48, 137.17, 128.62, 127.69, 127.45, 49.92
25b	152.71	149.37	119.25	156.11	138.72	88.65	77.45	63.19	72.69	65.75	153.40, 136.91, 128.46, 127.56, 127.23, 49.47
26a	152.72	166.34	102.78	143.94		91.53	81.65	65.53	79.35	62.03	140.05, 129.77, 128.69, 53.05
27b	152.41	148.97	119.34	156.28	140.83	88.74	80.75	64.08	78.09	61.03	140.47, 128.26, 128.00, 126.74, 51.38
17a	152.83	166.22	103.88	144.29		92.43	77.99	58.81	77.24	61.27	
17b	152.25	147.73	119.03	155.28	141.60	89.32	79.57	57.47	77.92	60.99	

[a] Solvents: DMSO-d_6, except for **10a** and **10b** ($CDCl_3$), **12a**, **12b**, **17a**, **22**, and **26a** (CD_3OD), and **13b** and **17b** (D_2O). ^{13}C-NMR signals of the sugar moiety were identificated on the basis of their $^1J_{C-H}$ coupling constants (see: Seela, F.; Stecker, H. *Helv. Chim. Acta* **1985**, *68*, 563) and by means of INEPT experiments. Other signals were assigned in comparison with those reported in *^{13}C-NMR spectral data*; Verlag-Chemie: Weinheim, 1981.

Table 3. Results of ^{1}H-NMR NOE Experiments[a]

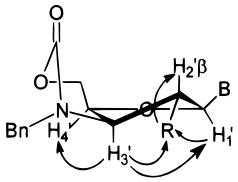
compound	signal irradiated	signal enhanced	measured enhancement (%)
10b	H2′α	H3′	5.0
	H4′	H3′	3.2
11	H2′α	H3′	9.2
	H4′	H3′	5.6
25a	H4′	H3′	7.0
25b	H4′	H3′	4.3
	H2′	H3′	0.8

[a] Solvents: DMSO-d_6, except for **10b** ($CDCl_3$ degassed by the freeze−pump−thaw procedure). For signal assignment, see: Table 1. H2′α in **10b** and **11** presented NOE effect when the H1′ signal was saturated (5 and 4.1%, respectively).

Synthesis of 3′-Amino-3′-deoxyxylonucleosides 17a,b. We tried to prepare the 3′-amino-3′-deoxyxylonucleosides in a manner similar to that followed for the synthesis of compounds **13a,b**. For this reason, we synthesized the corresponding 5′-*O*-(*N*-benzylcarbamoyl)-2′,3′-sulfonylated derivatives **15a,b** (see Scheme 4).

The uridine derivatives **15a** (R = Ms or Ts) always gave rise, under basic conditions (NaH in THF), to the 2,2′-anhydronucleosides **18** instead of the cyclic carbamates **16a**. These 2,2′-anhydronucleosides are so easily formed that no chance for fomation of products **16a** exists.

Chart 1

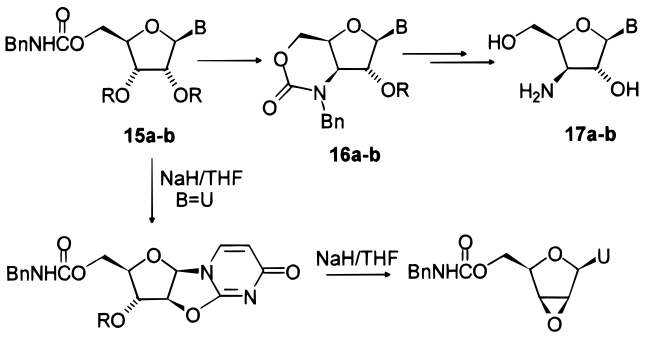


10b: R=H_2'α, B=Th
11: R=H_2'α, B=Ad
25a: R=OH, B=U
25b: R=OH, B=Ad

We tried to force the still 3′-activated 2,2′-anhydronucleosides **18** (R = Ms or Ts) to react, adding a second equivalent of NaH, but we observed the appearance of two other products, containing a 2′,3′-*lyxo*-epoxide structure and differing only in the base substitution (one of them was shown to be compound **19**). The 2′,3′-epoxylyxosyl structure probably arises from cleavage of the 2,2′-anhydronucleoside bond, as it has been proposed by other authors.[12]

(12) Yung, N. C.; Burchenal, J. H.; Fecher, R.; Duschinsky, R.; Fox, J. J. *J. Am. Chem. Soc.* **1961**, *83*, 4060.

Scheme 4



On the other hand, when the same methodology was applied to the purine nucleosides, which did not present the problem of the easy anhydronucleoside formation, we could see that the reactions were even more complicated. Thus, when **15b** (R = Ms or Ts) were treated with NaH in THF, mixtures of several unidentified products appeared. The ^{13}C-NMR spectra of those mixtures revealed the presence of several carbonyl signals around δ 206.[13]

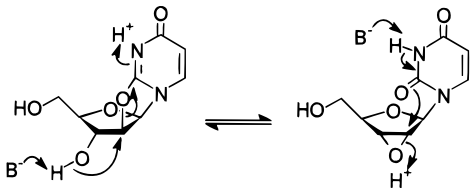
In an attempt to determine whether the lack of formation of product **16b** was due to conformational reasons, we decided to perform the reaction in other anhydrous organic solvents which could drive the conformational equilibrium of the sugar ring toward a more favorable situation for intramolecular nucleophilic substitution. The conformation of the sugar ring of **15a,b** (with R = Ms or Ts) was roughly studied by measuring the $^{3}J_{H-H}$ coupling constants between several hydrogen atoms of the carbohydrate in different deuterated solvents ($CDCl_3$, acetone-d_6, CD_3OD, and DMSO-d_6). This brief study showed that, for instance, the $^{3}J_{H1'-H2'}$ coupling constant increased with the polarity of the solvent (from around 2 Hz in $CDCl_3$ to 5−7 Hz in DMSO-d_6), regardless of the R group and the base present. This may be interpreted to be due to a shift of the averaged sugar conformation toward dispositions closer to the C2′ endo conformation (where the dihedral angle between both the H1′ and H2′ is closer to the 180° value). This conformation would favor the intramolecular nucleophilic attack from the neighboring 5′-position. However, when the reactions were performed in these solvents, the same results as those in THF were obtained.

A new strategy for the synthesis of the 3′-amino-3′-deoxyxylonucleosides had to be devised. Some reported results served as a good guide. In 1958, Brown *et al.* showed that the reaction of 2,2′-anhydrouridine with sodium ethyl sulfide gave 3′-deoxy-3′-ethylthioxylouridine, this result presumably arising from intervention of the 2′,3′-riboepoxide.[14] Later, it was proposed that the 2,2′-anhydronucleoside and the riboepoxide may be regarded as tautomers, with the equilibrium shifted by the basicity of the medium (see Scheme 5).[15]

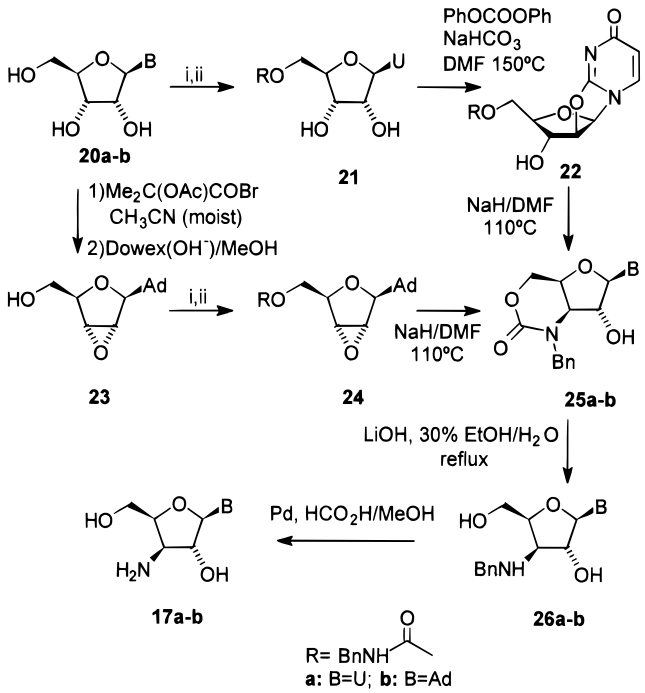
Taking this into account, we believed that a good way to deliver the amino function to the 3′-position from the neighboring 5′-*O*-(*N*-benzylcarbamoyl) group would be to drive that equilibrium toward the 2′,3′-riboepoxide, which subsequently would suffer intramolecular cyclization from the 5′-position to give the desired product. In fact, when the 2,2′-anhydronucleoside **22**, synthesized from the carbamate **21**,[16] was heated with a slight excess of sodium hydride in anhydrous DMF, the desired product **25a** was formed in a fast and quantitative manner (see Scheme 6). The structure of this cyclic carbamate was confirmed by ^{1}H- and ^{13}C-NMR spectra (see Tables 1 and 2). In order to corroborate the correct assignment of the ^{13}C-NMR spectra, a ^{1}H−^{13}C heteronuclear correlation experiment was performed. This showed the crosspeak between the ^{13}C signal at 63 ppm and the ^{1}H signal at 3.97 ppm corresponding to the H3′ hydrogen atom. Furthermore, the relative configuration of the sugar was confirmed by NOE experiments (see Table 3), as for the 2′-deoxynucleosides. The H3′ signal was enhanced by 7.0% when H4′ signal was irradiated. However, irradiation of H2′ gave no enhancement of H3′ signal, indicating their relative *trans* disposition.

In the case of purine ribonucleosides, the possibility of establishing the tautomeric equilibrium 2′,3′-riboep-

Scheme 5



Scheme 6



(i) CH_2=CHOCOON=CMe_2 , THF, CAL. (ii) $PhCH_2NH_2$, THF, reflux.

(13) 2′-Keto-3′-deoxy nucleosides have been described to be formed from compounds similar to **15a,b** through base-catalyzed desulfonyloxylation−desulfonylation reactions: (a) Sasaki, T.; Minamoto, K.; Suzuki, H. *J. Org. Chem.* **1973**, *38*, 598. (b) Sasaki, T.; Minamoto, K.; Tanizawa, S. *J. Org. Chem.* **1973**, *38*, 2896. (c) Kawana, M.; Kuzuhara, H. *Tetrahedron Lett.* **1987**, *28*, 4075. (d) An alternative explanation would be an initial desulfonylation followed by a [1,2]-hydride shift rearrangement with Walden displacement of the remaining sulfonate: Hansske, F.; Robins, M. J. *J. Am. Chem. Soc.* **1983**, *105*, 6736.

(14) Brown, D. M.; Parihar, D. B.; Todd, A.; Varadarajan, S. *J. Chem. Soc.* **1958**, 3028.

(15) Chattopadhyaya, J. B.; Reese, C. B. *J. Chem. Soc., Chem. Commun.* **1976**, 860.

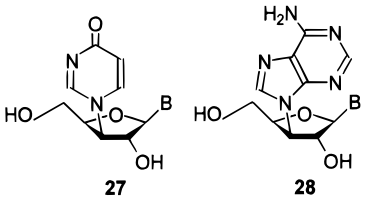
(16) (a) Hampton, A.; Nichol, A. W. *Biochemistry* **1966**, *5*, 2076. (b) We chose the procedure described in ref 16a instead of the one followed by Verheyden *et. al.*[2c] Despite the fact that HMPT solvent gives better results than DMF in this kind of reactions (88 *vs* 59% yield of 2,2′-anhydrouridine from uridine), we preferred not to use this toxic solvent.

Table 4. Isolated Global Yields[a]

starting nucleoside	carbamate (%)	alkylamino nucleoside (%)	amino nucleoside (%)
1 B = Th	**10a** (62)	**12a** (53)	
1 B = Th	**10b** (64)	**12b** (57)	**13a** (56)
1 B = Ad	**11** (46)	**14** (37)	**13b** (34)
20a	**25a** (54)	**26a** (46)	**17a** (44)
20b	**25b** (66)	**26b** (49)	**17b** (45)

[a] Calculated with respect to the starting material.

Chart 2



B= Ad, C, G, U

oxide ↔ anhydronucleoside is restricted to 8-oxyadenosine derivatives.[15] However, the high yield synthesis of the riboepoxide **23** can be easily achieved by means of the procedure described by Robins *et al*.[17] Carbamate **24** was then obtained and heated with NaH in DMF to yield the corresponding cyclic carbamate **25b** almost quantitatively (see Table 3 for data about NOE experiments performed on this compound).[18]

Subsequent decarbonylation of **25a,b** with LiOH and catalytic transfer hydrogenation of the resulting compounds **26a,b** yielded the corresponding 3′-amino-3′-deoxyxylouridine **17a** and 3′-amino-3′-deoxyxyloadenosine **17b** (see Tables 1 and 2 for ^{1}H- and ^{13}C-NMR spectral data of these and the preceding compounds).[2e] Once again, the most remarkable difference is the upfield shift of *ca*. 12 ppm of the C3′ carbon atom signal with regard to the starting ribonucleosides.

Summary

Table 4 summarizes the results obtained with respect to the starting natural ribonucleosides and 2′-deoxyribonucleosides. As can be seen, final aminosugar nucleosides are attained with yields ranging from 30 to 55%.

In conclusion, we have presented a novel approach to the synthesis of 3′-aminoxylonucleosides that involves the intramolecular delivery of the masked amino nucleophile from the 5′-position regiospecifically to the 3′-position of the sugar.

The described aminosugar nucleosides are unique precursors for isonucleoside analogs of the general structure **27** and **28** (Chart 2). The synthesis and pharmacological evaluation of several of these compounds will be reported in the near future.

Experimental Section

General. Lipase from *C. antarctica* SP 435L (8.200 PLU/g), generously donated by Novo Nordisk Company, was kept for 2 days under vacuum prior to use. Nucleosides and other chemicals were purchased from Sigma and Aldrich Chemie, and solvents were distilled. THF and DMF were dried by reflux over and distillation from sodium and CaH_2, respectively. Pyridine was freshly distilled from KOH. Acetone *O*-(phenyloxycarbonyl)oxime was prepared by treating acetone oxime with phenylchloroformate and purified by conventional procedures. 1H-NMR data listed in the following manner: chemical shift (multiplicity, number of protons, assignment). For other experimental details, see ref 8c.

Enzymatic Synthesis of 5′-*O*-((Phenyloxy)carbonyl)-thymidine (2) [Procedure A]. One millimole of **1** (B = Th), 3 mmol of acetone *O*-((phenyloxy)carbonyl)oxime, and 0.4 g of lipase from *C. antarctica* (CAL) were suspended in 20 mL of THF. The mixture was allowed to react at 60 °C and 250 rpm for 36 h (monitored by TLC until almost complete disappearance of **1**). Then, the enzyme was filtered and washed with MeOH, and the residue was evaporated under vacuum and subjected to flash chromatography (AcOEt) to yield **2** (0.29 g, 80%): mp 163−164 °C; IR (KBr, cm^{-1}) 1767; ^{1}H NMR (CD_3OD) δ 7.81 (s, 1, H6), 7.62 (m, 2, Ph), 7.48 (m, 1, Ph), 7.39 (m, 2, Ph), 6.52 (t, 1, H1′), 4.69 (m, 2, H5′,5″), 4.64 (m, 1, H3′), 4.33 (m, 1, H4′), 2.59−2.42 (m, 2, H2′,2″), 2.02 (s, 3, Me); ^{13}C NMR (CD_3OD) δ 166.83 (C4), 155.38 (C=O), 153.04 (Ph), 152.78 (C2), 138.14 (C6), 131.15 (Ph), 127.83 (Ph), 122.61 (Ph), 112.30 (C5), 86.89 (C1′), 86.02 (C4′), 72.48 (C3′), 69.41 (C5′), 41.14 (C2′), 13.05 (Me); MS (70 eV), *m*/*z* (rel intensity) 362 (M^+, 1), 237 (6), 94 (100). Anal. Calcd for $C_{17}H_{18}N_2O_7$: C, 49.72; H, 4.97; N, 7.73. Found: C, 49.65; H, 5.10; N, 7.62.

5′-*O*-((Vinyloxy)carbonyl)adenosine (3). Treatment of 1 mmol of 2′-deoxyadenosine **1** (B = Ad) by procedure A (using acetone *O*-((vinyloxy)carbonyl)oxime and performing the reaction during 8 h at 30 °C) gave **3** (243 mg, 78%) after chromatography (AcOEt−MeOH 92:8).[8c]

General Procedure for the Synthesis of the 5′-*O*-(*N*-Alkylcarbamoyl)-3′-*O*-methylsulfonyl(and 3′-*O*-*p*-toluenesulfonyl)-2′-deoxynucleosides (5b, 6a,b, 8a,b). A solution of carbonate **2** or **3** (2 mmol) and the corresponding amine (8 mmol) in 15 mL of THF was stirred at reflux until no starting material was detected by TLC (less than 1 day). Solvent and most of the amine were then removed by evaporation under vacuum. The residue was precipitated and washed several times by addition of ethyl ether (for the 2′-deoxyadenosine derivatives, the residue was submitted to flash chromatography, AcOEt−MeOH 9:1). Some of these intermediate carbamates have been previously described by us.[8c] They were dissolved in 10 mL of dry pyridine and treated with 6 mmol of the corresponding sulfonyl chloride (in the case of the *p*-toluenesulfonyl derivatives, an additional 2 mmol of *p*-toluenesulfonyl chloride were added 10 h later to complete the reaction). The mixture was stirred overnight, and the reaction stopped by addition of 1 mL of ice water when complete by TLC (about 15−20 h). The pyridine was then carefully evaporated. Water (30 mL) was added to the residue, and the solution was extracted (CH_2Cl_2, 2 × 50 mL). The combined organic phase was washed twice with 5% $NaHCO_3$ and with water, dried, filtered, and evaporated to give products **5b** (860 mg, 90%), **6a** (760 mg, 84%), **6b** (845 mg, 80%), and **8a** (740 mg, 80%), as colorless foams. For compound **8b**, the solid obtained was chromatographed (AcOEt−MeOH 91:9), due to the appearance of derivatives resulting from tosylation of the adenine base. Compound **8b** was obtained in 55% yield (592 mg).

For **5b**: mp softened at 68 °C (the compound does not have a clear melting point) ; IR (KBr, cm^{-1}) 1709; ^{1}H NMR ($CDCl_3$) δ 7.77 (d, 2, Ts), 7.31 (d, 2, Ts), 7.12 (s, 1, H6), 6.10 (t, 1, H1′), 5.75 (m, 1, CH), 5.58 (m, 1, H3′), 5.11 (dd, 1, CH_2), 5.02 (dd, 1, CH_2), 4.24−4.02 (m, 2, H5′,5″), 4.23 (m, 1, H4′), 3.70 (m, 1, CH_2), 2.45 (m, 1, H2′), 2.39 (s, 3, MePh), 2.18 (m, 1, H2″), 1.86 (s, 3, Me); ^{13}C NMR ($CDCl_3$) δ 164.03 (C4), 155.35 (C=O), 150.23 (C2), 145.43 (Ts), 136.06 (C6), 135.19 (CH), 132.61 (Ts), 129.96 (Ts), 127.57 (Ts), 116.05 (CH_2), 110.89 (C5), 85.28 (C1′), 81.99 (C4′), 79.87 (C3′), 63.36 (C5′), 43.27 (CH_2), 37.43 (C2′), 21.46 (MePh), 12.33 (Me); MS (70 eV), *m*/*z* (rel intensity) 479 (M^+, 10), 307 (10). Anal. Calcd for $C_{21}H_{25}N_3O_8S$: C, 52.60; H, 5.26; N, 8.76. Found: C, 52.52; H, 5.18; N, 8.70. For **6a**: mp softened at 80 °C (the compound does not have a clear melting point); IR (KBr, cm^{-1}) 1706; ^{1}H NMR (CD_3OD) δ 7.61

(17) Robins, M. J.; Wilson, J. S.; Madej, D.; Low, N. H.; Hansske, F.; Wnuk, S. F. *J. Org. Chem*. **1995**, *60*, 7902.

(18) A simpler synthetic scheme would be to treat compound **23** with benzyl isocyanate and follow the same synthetic scheme. However, this sequence has been rejected, since the last step of hydrogenation of the analog of product **26b**, containing a *N*-benzylcarbamoyl group attached to the exocyclic amino group of the adenine, did not give the expected results.

(s, 1, H6), 7.49 (m, 5, Ph), 6.46 (dd, 1, H1′), 5.52 (m, 1, H3′), 4.61 (m, 1, H4′), 4.58−4.48 (m, 2, H5′,5″), 4.49 (d, 2, CH_2), 3.38 (s, 3, Me), 2.79 (m, 1, H2′), 2.65 (m, 1, H2″), 1.95 (s, 3, Me); ^{13}C NMR (CD_3OD) δ 166.63 (C4), 158.64 (C=O), 152.62 (C2), 140.73 (Ph), 137.78 (C6), 130.01 (Ph), 128.85 (Ph), 128.76 (Ph), 112.45 (C5), 86.84 (C1′), 84.33 (C4′), 82.32 (C3′), 65.55 (C5′), 46.06 (CH_2), 38.99 (C2′), 38.78 (Me), 13.12 (Me); MS (70 eV), *m/z* (rel intensity) 453 (M^+, 1), 357 (10), 150 (50), 91 (100). Anal. Calcd for $C_{19}H_{23}N_3O_8S$: C, 50.33; H, 5.11; N, 9.27. Found: C, 50.21; H, 5.06; N, 9.35. For **6b**: mp 151−154 °C; IR (KBr, cm^{-1}) 1707; ^{1}H NMR ($CDCl_3$) δ 7.76 (d, 2, Ts), 7.35 (d, 2, Ts), 7.25 (m, 5, Ph), 7.15 (s, 1, H6), 6.11 (t, 1, H1′), 5.10 (m, 1, H3′), 4.30−4.10 (m, 2, H5′,5″), 4.30 (m, 1, H4′), 4.28 (d, 2, CH_2), 2.41 (s, 3, MePh), 2.40 (m, 1, H2′), 2.25 (m, 1, H2″), 1.70 (s, 3, Me); ^{13}C NMR ($CDCl_3$) δ 163.92 (C4), 155.50 (C=O), 150.13 (C2), 145.31 (Ts), 137.88 (Ph), 135.31 (C6), 132.48 (Ts), 129.84 (Ts), 128.23 (Ph), 127.44 (Ph), 127.09 (Ts), 110.73 (C5), 85.16 (C1′), 81.81 (C4′), 79.84 (C3′), 63.32 (C5′), 44.64 (CH_2), 37.15 (C2′), 21.31 (MePh), 12.07 (Me); MS (70 eV), *m/z* (rel intensity) 529 (M^+, 5), 396 (10), 357 (20). Anal. Calcd for $C_{25}H_{27}N_3O_8S$: C, 56.70; H, 5.14; N, 7.93. Found: C, 56.43; H, 5.00; N, 7.90. For **8a**: mp 185−187 °C; IR (KBr, cm^{-1}) 1718; ^{1}H NMR ($CDCl_3$) δ 8.09 (s, 1, H8), 7.83 (s, 1, H2), 7.23 (m, 5, Ph), 6.29 (t, 1, H1′), 5.50 (m, 1, H3′), 4.41 (m, 1, H4′), 4.40−4.25 (m, 2, H5′,5″), 4.38 (d, 2, CH_2), 3.10 (m, 1, H2′), 3.08 (s, 3, Me), 2.70 (m, 1, H2″); ^{13}C NMR ($CDCl_3$) δ 155.87 (C6), 155.53 (C=O), 152.64 (C2), 148.87 (C4), 138.94 (C8), 138.02 (Ph), 128.35 (Ph), 127.13 (Ph), 119.47 (C5), 83.87 (C1′), 82.22 (C4′), 79.19 (C3′), 62.87 (C5′), 44.72 (CH_2), 38.01 (Me), 38.96 (C2′); MS (70 eV), *m/z* (rel intensity) 462 (M^+, 20), 366 (20), 119 (30). Anal. Calcd for $C_{19}H_{22}N_6O_6S$: C, 49.34; H, 4.79; N, 18.17. Found: C, 49.22; H, 4.76; N, 18.05. For **8b**: mp 166−168 °C; IR (KBr, cm^{-1}) 1720; ^{1}H NMR ($CDCl_3$) δ 8.07 (s, 1, H8), 7.82 (s, 1, H2), 7.75 (d, 2, Ts), 7.29 (d, 2, Ts), 7.20 (m, 5, Ph), 6.25 (t, 1, H1′), 5.43 (m, 1, H3′), 4.30 (m, 1, H4′), 4.25−4.15 (m, 2, H5′,5″), 4.22 (d, 2, CH_2), 2.95 (m, 1, H2′), 2.51 (m, 1, H2″), 2.30 (s, 3, MePh); ^{13}C NMR ($CDCl_3$) δ 155.58 (C6), 155.52 (C=O), 152.43 (C2), 148.77 (C4), 145.22 (Ts), 138.94 (C8), 137.94 (Ph), 132.39 (Ts), 129.76 (Ts), 128.18 (Ph), 127.74 (Ph), 127.07 (Ts), 119.44 (C5), 83.91 (C1′), 81.99 (C4′), 79.87 (C3′), 63.03 (C5′), 44.57 (CH_2), 36.50 (C2′), 21.26 (MePh); MS (70 eV), *m/z* (rel intensity) 538 (M^+, 20), 369 (70). Anal. Calcd for $C_{25}H_{26}N_6O_6S$: C, 55.75; H, 4.87; N, 15.60. Found: C, 55.59; H, 4.80; N, 15.48.

3′-*N*-Allylamino-3′-deoxyxylothymidine 3′,5′-Carbamate (10a). A solution of 0.86 g (1.8 mmol) of **5b** in 15 mL of dry THF was treated with a suspension of 0.13 g (5.4 mmol) of NaH in THF (15 mL). The resulting mixture was stirred under nitrogen atmosphere at 25 °C for 20 h (until **5b** completely disappeared by TLC), at which point solvent was carefully removed under vacuum and the resulting residue was submitted to flash chromatography (AcOEt−MeOH 82:18) to afford **10a** (480 mg, 87%): mp 156−158 °C; IR (KBr, cm^{-1}) 1693; MS (70 eV), *m/z* (rel intensity) 307 (M^+, 40), 182 (100). Anal. Calcd for $C_{14}H_{17}N_3O_5$: C, 54.72; H, 5.58; N, 13.67. Found: C, 54.69; H, 5.56; N, 13.60.

3′-*N*-Benzylamino-3′-deoxyxylothymidine 3′,5′-Carbamate (10b). From **6a**: A solution of 136 mg (0.3 mmol) of **6a** in 2.5 mL of dry THF was cooled to 0 °C and treated with a suspension of 22 mg (0.9 mmol) of NaH in THF (2.5 mL). The cooling bath was removed after 2 h, and the reaction was continued at room temperature and under N_2 atmosphere for 20 h (until **6a** completely disappeared), at which point solvent was evaporated under vacuum. The residue was treated with 10 mL of 10% NH_4Cl solution and extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were washed twice with 5% $NaHCO_3$ solution, once with water, dried (Na_2SO_4), filtered, and concentrated to afford **10b** (75 mg, 70%): mp 194−196 °C; IR (KBr, cm^{-1}) 1691; MS (70 eV), *m/z* (rel intensity) 357 (M^+, 20), 232 (40), 91 (100). Anal. Calcd for $C_{18}H_{19}N_3O_5$: C, 60.50; H, 5.36; N, 11.76. Found: C, 60.43; H, 5.30; N, 11.55.

From **6b**: A solution of 582 mg (1.1 mmol) of **6b** in 10 mL of dry THF was cooled to 0 °C and treated with a suspension of 84 mg (3.5 mmol) of NaH in THF (10 mL). The cooling bath was removed after 2 h, and the reaction was continued at room temperature and under N_2 atmosphere for 5 h. Solvent was then removed under vacuum. The resulting residue was treated with 30 mL of 10% NH_4Cl solution and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed twice with 5% $NaHCO_3$ solution, once with water, dried (Na_2SO_4), filtered, and concentrated to afford **10b** (360 mg, 92%).

3′-*N*-Benzylamino-2′,3′-dideoxyxyloadenosine 3′,5′-Carbamate (11). From **8a**: A solution of 370 mg (0.8 mmol) of **8a** in 10 mL of dry THF was treated with a suspension of 77 mg (3.2 mmol) of NaH in THF (10 mL) at 30 °C under N_2 atmosphere. The reaction was continued for 4 h, and then 5 mL of MeOH were added to the solution. Solvent was evaporated under vacuum, and the residue was chromatographed (AcOEt−MeOH 8:2). Appropriate fractions were combined and evaporated to give **11** (216 mg, 74%): mp 236−238 °C; IR (KBr, cm^{-1}) 1690; MS (70 eV), *m/z* (rel intensity) 366 (M^+, 70), 136 (100), 91 (100). Anal. Calcd for $C_{18}H_{18}N_6O_3$: C, 59.01; H, 4.95; N, 22.94. Found: C, 58.95; H, 4.88; N, 22.79.

From **8b**: A solution of 377 mg (0.7 mmol) of **8b** in 8 mL of dry THF was cooled to 0 °C and treated with a suspension of 68 mg (2.8 mmol) of NaH in THF (8 mL). The reaction was stirred under N_2 atmosphere for 3 h, at which point 5 mL of MeOH were added. The solvent was evaporated under vacuum, and the residue was chromatographed (AcOEt−MeOH 8:2). The product was concentrated to give **11** (235 mg, 92%).

3′-*N*-Allylamino- and 3′-*N*-Benzylamino-2′,3′-dideoxyxylonucleosides (12a,b, 14) [Procedure B]. One millimole of **10a,b** or **11** was dissolved in 30% aqueous EtOH (20 mL). LiOH (800 mg, 33.3 mmol) was added, and the mixture was heated at reflux for 1−3 h (until TLC revealed complete disappearance of the starting nucleoside). Solvents were removed under vacuum, and the precipitate was eluted with CH_2Cl_2−MeOH 9:1 through a pad of silica gel (CH_2Cl_2−MeOH 85:15 in the case of product **12a**). For **12a** (238 mg, 85%): mp softened at 85 °C (the compound does not have a clear melting point); IR (KBr, cm^{-1}) 1695; MS, *m/z* (FAB^+, rel intensity) 282 (M + H, 70)$^+$, 154 (100). Anal. Calcd for $C_{13}H_{19}N_3O_4$: C, 55.51; H, 6.81; N, 14.94. Found: C, 55.43; H, 6.77; N, 14.79. For **12b** (298 mg, 90%): mp 141−143 °C; IR (KBr, cm^{-1}) 1674; MS (70 eV), *m/z* (rel intensity) 331 (M^+, 20), 224 (60), 91 (100). Anal. Calcd for $C_{17}H_{21}N_3O_4$: C, 61.62; H, 6.39; N, 12.68. Found: C, 61.58; H, 6.30; N, 12.61. For **14** (275 mg, 81%): mp 151−153 °C; IR (KBr, cm^{-1}) 1676; MS (70 eV), *m/z* (rel intensity) 340 (M^+, 10), 235 (60), 136 (60), 91 (100). Anal. Calcd for $C_{17}H_{20}N_6O_2$: C, 59.99; H, 5.92; N, 24.69. Found: C, 59.85; H, 5.80; N, 24.48.

3′-Amino-3′-deoxyxylothymidine (13a) [Procedure C].[10] The benzyl derivative **12b** (100 mg) dissolved in 5 mL of 4.4% formic acid−methanol was added to a 5 mL round-bottom flask containing 100 mg of palladium black catalyst and 5 mL of 4.4% formic acid−methanol. The mixture was continuously stirred under a nitrogen atmosphere. Reaction was complete within 40−60 min as determined by thin layer chromatography analysis of samples taken at different times. Products were isolated by filtering off with a pad of Celite, and the pad was washed well with MeOH. Solvent was removed in vacuo, and the resulting residue was dissolved in 3% HCl/MeOH. The solvent was then removed to give the HCl salt of **13a** (82 mg, 98%).[4]

3′-Amino-2′,3′-dideoxyxyloadenosine (13b). Treatment of product **14** (100 mg) by procedure C in the presence of a large excess of palladium black catalyst (1 g), showed after 1 h complete absence of the starting material. Careful filtration was performed, washing the catalyst several times with MeOH. The residue obtained after evaporation of the solvent was dissolved in 2 mL of 3% HCl/MeOH, and the solvent was removed to give the HCl salt of **13b** (77 mg, 92%):[2h] MS, *m/z* (FAB^+, rel intensity) 251 (M + H, 85)$^+$, 136 (100).

5′-*O*-(*N*-Benzylcarbamoyl)uridine (21). Treatment of uridine **20a** (244 mg, 1 mmol) with acetone *O*-((vinyloxy)-carbonyl)oxime by procedure A at 60 °C, gave after 24 h a mixture of two products, as shown by thin layer chromatography analysis. After filtration of the catalyst and evaporation of the solvent, the residue was subjected to flash chromatography (AcOEt−MeOH 9:1) and two different products were collected. The less polar product was the 5′-*O*-((vinyloxy)-

carbonyl) uridine derivative (195 mg, 62%), as shown by ^{1}H NMR analysis, while the other one was the 5′-acetonoxime carbonate (125 mg, 36%). Both products were dissolved in dry THF (8 mL) and treated with 4 mmol of benzylamine. The solution was stirred at reflux temperature for 5 h, at which point the solvent and most of the remaining amine were evaporated in vacuo. Flash chromatography (AcOEt−MeOH 9:1) of the resulting residue yielded **21** (320 mg, 85%).[8c]

2,2′-Anhydro-1-[5-*O*-(*N*-benzylcarbamoyl)-*β*-D-arabinofuranosyl]uracil (22). Uridine carbamate **21** (4 mmol, 1.51 g) was dissolved in dry DMF (4 mL) and treated with diphenyl carbonate (1.1 g, 5.15 mmol) and $NaHCO_3$ (20 mg).[16] The mixture was heated at 150 °C for 5 min, the solvent was evaporated under vacuum and the resulting gum was chromatographed (AcOEt−MeOH 85:15) to yield **22** (1.0 g, 70%): mp 144−145 °C; IR (KBr, cm^{-1}) 1720; MS (70 eV), *m*/*z* (rel intensity) 359 (M$^+$, 5), 248 (10), 91 (100). Anal. Calcd for $C_{17}H_{17}N_3O_6$: C, 56.82; H, 4.77; N, 11.69. Found: C, 56.74; H, 4.75; N, 11.61.

3′-*N*-Benzylamino-3′-deoxyxylouridine 3′,5′-Carbamate (25a). 2,2′-Anhydrouridine derivative **22** (198 mg, 0.55 mmol) was dissolved in dry DMF (5 mL) and treated with NaH (40 mg, 1.6 mmol). The mixture was heated under nitrogen atmosphere at 100−110 °C for 10 min, at which point the solvent was evaporated under vacuum. Flash chromatography of the resulting residue (AcOEt−MeOH 9:1) yielded a colorless solid identified as **25a** (180 mg, 91%): mp 234−237 °C; IR (KBr, cm^{-1}) 1695; MS (70 eV), *m*/*z* (rel intensity) 359 (M$^+$, 10), 189 (20), 91 (70), 44 (100). Anal. Calcd for $C_{17}H_{17}N_3O_6$: C, 56.82; H, 4.77; N, 11.69. Found: C, 56.78; H, 4.79; N, 11.56.

9-[2,3-Anhydro-5-*O*-(*N*-benzylcarbamoyl)-*β*-D-arabinofuranosyl]adenine (24). Treatment of **23** (200 mg, 0.8 mmol)[17] with acetone *O*-((vinyloxy)carbonyl)oxime (2.4 mmol) in 20 mL of THF in presence of 0.4 g of CAL at 60 °C gave after 24 h complete disappearance of the starting material. A batch of seven reactions like this were performed at the same time (1.4 g, 5.6 mmol of **23**). After filtration of the catalyst and evaporation of the solvent, the total residue was subjected to flash chromatography (CH_2Cl_2−MeOH 95:5). A mixture of two products was obtained (5′-vinyl and 5′-acetonoxime carbonates), concentrated (1.72 g), dissolved in dry THF (30 mL), and treated with 16.8 mmol of benzylamine. The solution was stirred at reflux temperature for 8 h. The solvent and most of the remaining amine were then removed by evaporation *in vacuo*. The resulting gum was precipitated and washed with EtOH (4 × 4 mL) to give 1.6 g of a white solid. Evaporation of the filtrate and precipitation with EtOH yielded 0.15 g more of the same colorless solid **24** (1.75 g, 82%): mp 166−168 °C; IR (KBr, cm^{-1}) 1690; MS (70 eV), *m*/*z* (rel intensity) 382 (M$^+$, 5), 248 (10), 91 (100). Anal. Calcd for $C_{18}H_{18}N_6O_4$: C, 56.54; H, 4.74; N, 21.98. Found: C, 56.48; H, 4.76; N, 21.84.

3′-*N*-Benzylamino-3′-deoxyxyloadenosine 3′,5′-Carbamate (25b). A solution of 191 mg (0.5 mmol) of **24** was dissolved in dry DMF (5 mL) and treated with NaH (36 mg, 1.5 mmol). The mixture was heated under nitrogen atmosphere at 100−110 °C for 10 min, at which point the solvent was evaporated under vacuum and the resulting residue was submitted to flash chromatography (AcOEt−MeOH 9:1) to afford **25b** (168 mg, 88%): mp softened at 135 °C (the compound does not have a clear melting point but slowly colorized above 160 °C); IR (KBr, cm^{-1}) 1691; MS (70 eV), *m*/*z* (rel intensity) 382 (M$^+$, 10), 164 (100), 136 (90). Anal. Calcd for $C_{18}H_{18}N_6O_4$: C, 56.54; H, 4.74; N, 21.98. Found: C, 56.41; H, 4.66; N, 21.87.

3′-*N*-Allylamino- and 3′-*N*-Benzylamino-3′-deoxyxylonucleosides (26a,b). Treatment of 1 mmol of **25a,b** by procedure B gave after 1−2 h complete disappearance of the starting material. The solvents were removed under vacuum, and the residue was chromatographed through a pad of silica gel first with CH_2Cl_2−MeOH 9:1 and finally with MeOH. For **26a** (286 mg, 86%): mp 189−192 °C; IR (KBr, cm^{-1}) 1690; MS (70 eV), *m*/*z* (rel intensity) 333 (M$^+$, 1), 204 (20), 91 (100). Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61. Found: C, 57.58; H, 5.73; N, 12.49. For **26b** (267 mg, 75%): mp 162−164 °C; IR (KBr, cm^{-1}) 1649; MS, *m*/*z* (FAB$^+$, rel intensity) 357 (M + H, 95)$^+$, 136 (100). Anal. Calcd for $C_{17}H_{20}N_6O_3$: C, 57.29; H, 5.66; N, 23.58. Found: C, 57.17; H, 5.59; N, 23.40.

3′-Amino-3′-deoxyxylonucleosides (17a,b). Treatment of products **26a,b** (100 mg) by procedure C (for the debenzylation of the adenosine derivative **26b**, a great excess of palladium black catalyst (1 g) had to be used) showed after 1 h complete absence of the starting material. Products were isolated by filtering the catalyst with a pad of Celite, and the pad was washed well with MeOH. Solvent was then removed *in vacuo*. The resulting residue was dissolved in 3% HCl/MeOH, and the solvent was evaporated to give the HCl salt of **17a,b**. For **17a** (79 mg, 95%): mp softened at 70 °C (the compound does not have a clear melting point but slowly colorized above 150 °C); IR (KBr, cm^{-1}) 1693; MS, *m*/*z* (FAB$^+$, rel intensity) 244 (M + H, 60)$^+$, 136 (70). Anal. Calcd for $C_9H_{14}N_3O_5Cl$: C, 38.65; H, 5.05; N, 15.02. Found: C, 38.58; H, 4.99; N, 14.91. For **17b** (77 mg, 91%):[2e] MS, *m*/*z* (FAB$^+$, rel intensity) 267 (M + H, 55)$^+$, 136 (100).

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