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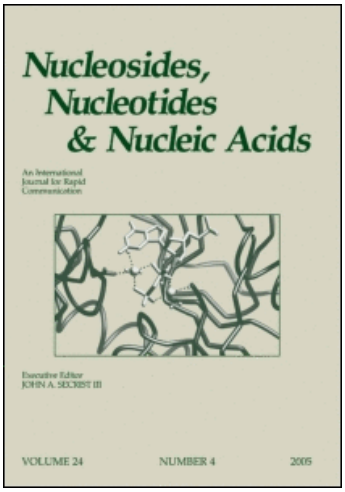

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Access to a New Type of Homo-*C*-Nucleosides with a "Split" 8-Deazapurine via a 1,3-Dipolar Cycloaddition Reaction

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NUCLEOSIDES & NUCLEOTIDES, 16(3), 291-300 (1997)

ACCESS TO A NEW TYPE OF HOMO-C-NUCLEOSIDES WITH A "SPLIT" 8-DEAZAPURINE *VIA* A 1,3-DIPOLAR CYCLOADDITION REACTION

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ABSTRACT: Upon a 1,3-dipolar addition reaction with trimethylsilyl acetylene, azides (*R,S*)-7 were converted to the triazoles (*R,S*)-8. These diastereoisomers were separated and individually protodesilylated to yield (*R*)- and (*S*)-9, fully characterized by NMR. Structural assignments of unsaturated side compounds were deduced from a QUIET-NOESY experiment. Compounds (*R*)- and (*S*)-9 represent a new type of homo-*C*-nucleosides with a "split" 8-azapurine base moiety.

INTRODUCTION

The adenine base, as found in nucleosides, can be considered as a bicyclic heterocycle consisting of a pyrimidine part and an imidazole ring, sharing one carbon-carbon bond. An hitherto unknown series of new nucleoside analogues are those where both heterocycle units are separated from each other. These structures may be named "split nucleosides". In this way the recognition elements for molecular interactions of the purine base are still present, but they are disconnected from each other. Such molecules can be considered as homo-*C*-nucleosides (*i.e.*, a class of compounds that possess a methylene unit between the ribose moiety and a sp^2-carbon of the nucleobase) with two heterocyclic rings on the methylene bridge. The synthesis and biological activity of various *C*-nucleosides has been described extensively in the past.[1] However, relatively little work has been done on the synthesis of the related homo-*C*-nucleosides. Here we report on the synthesis of the first "split nucleoside" as structural mimic of an 8-azapurine nucleoside.

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RESUTS AND DISCUSSION

The reaction of 2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranose (1) with α-chloro-α-(4-chloro-6-pyrimidinyl)methylenetriphenylphosphorane (**2**) has been previously reported to lead to mixtures of α and β anomers of 4-chloro-6-[chloro-(D-ribofuranosyl)methyl]-pyrimidine homo-*C*-nucleoside (**3**), together with minor amounts of the unsaturated derivatives (*E*)- and (*Z*)-**4**.[2] These configurational assignments have been proven to be partly erroneous by Herrera *et al.*[2] What the authors in ref 1 considered to be the α and β anomers of **3** were in fact β–(*R*)- and β–(*S*)-**3**, which are epimeric at the carbon bearing chlorine. By repeating the Wittig reaction between **1** and **2**, we confirmed the data as described in ref. 2. Treatment of the epimeric mixture (*R,S*)-**3** with saturated ammonia in methanol has been reported to lead to (*R,S*)-**5** and the corresponding 4-methoxypyrimidine analogues.[3] By using dioxane instead of methanol as solvent for the amino/halogen exchange reaction, the formation of the undesired methoxy-substituted products is prevented and the yield of (*R,S*)-**5** increases from 46 to 64%.

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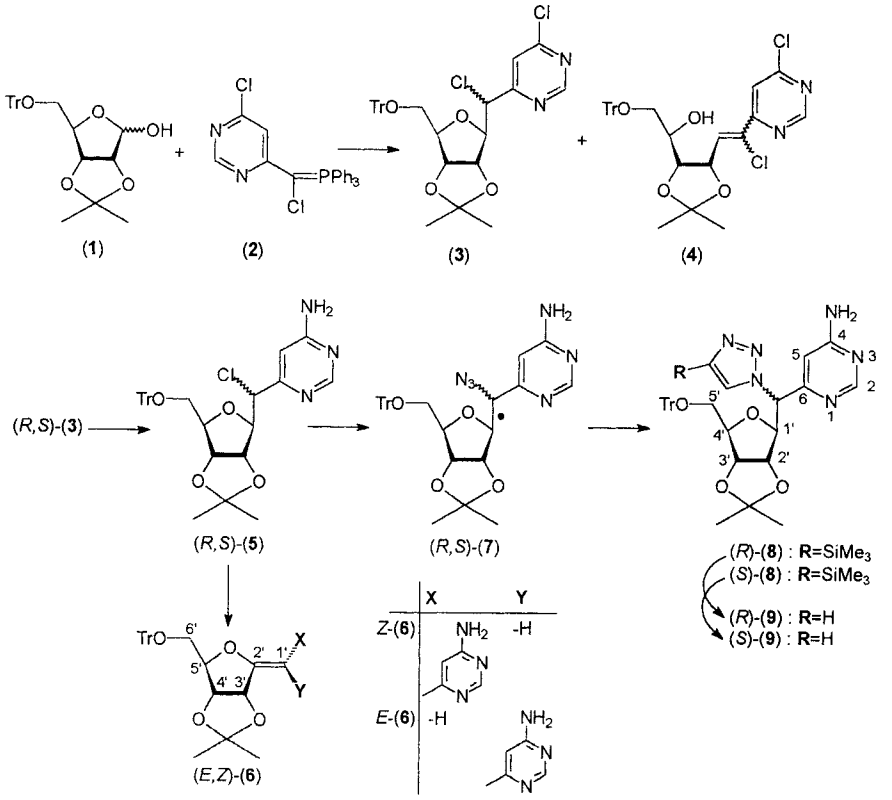

In an effort to obtain the imidazole substitution products, (*R,S*)-**5** was treated with the sodium salt of imidazole in DMF. However, the reaction products were characterized as the olefins (*E*)- and (*Z*)-**6**, in a 1:1 ratio. The assignment of the ^{1}H resonances of the ribose ring protons of (*E*)-**6** and (*Z*)-**6** was straightforward from the coupling pattern of the 1D-spectrum and, at least for (E)-**6**, confirmed from an absolute value COSY45 experiment at 200 MHz. For the base, two resonances were found at δ 8.53 and 7.14 ppm (values for (*E*)-**6**), which show a mutual long range coupling constant of 1.1 Hz, and were assigned to H-2 and H-5 respectively. The ^{13}C signals were assigned partly on the basis of their chemical shift and from a {^{13}C, ^{1}H} correlated spectrum. From the latter experiment the resonances of the ribose, of C-1', and of the base carbons C-2 and C-5 could be assigned with certainty. In the 160 ppm-region, characteristic for heteroatom-substituted sp^2-carbons, four resonances are seen. From an attached proton (APT)-test it follows that three are quaternary (C-2', C-4 and C-6) and one is tertiary (C-2). The discrimination between the former three was based on a comparison between a non-decoupled and a selectively at H-5 decoupled ^{13}C spectrum (doublets for C-6 and C-4 became singlets) combined with a long-range HETCOR experiment (long-range coupling visible between C-2' and H-1'/H-5', and between C-4/C-6 and H-2). The observed differences in ^{1}H NMR chemical shifts of both isomers, however, do not allow to derive double bond configuration since the position of the base with respect to the double bond (conformation C-1'–C-6 bond) nor the anisotropy of the base are known. Also the allylic long-range coupling constants between H-1' and H-3' do not allow differentiation, since they are identical in both isomers. Structural assignments were deduced from a QUIET-NOESY experiment. QUIET-NOESY[4,5] suppresses exchange or spin diffusion cross-peaks by inserting a double selective inversion pulse which inverts the regions around the two suspected protons (in the present case the region around NH_2 and H-5, H-1' being the proton that mediates diffusion), called "quiet windows". Although the authors[4,5] recommend a gaussian cascade inversion pulse,[4b] we used an i-SNOB-3 inversion pulse[6] on the resonances at δ 6.43 and 4.69 ppm. An unambiguous NOE effect between H-1' and H-3' is observed in the less polar isomer, while this correlation is missing for its polar counterpart. Consequently, the apolar isomer, with H-1' *syn* vs. H-3' (and the isopropylidene group), is assigned as (*Z*)-**6** (Figure 1).

Reaction of (*R,S*)-**5** with sodium azide in DMF at 90°C led to the expected substitution products (*R,S*)-**7** in good yield.[3] A thermally induced 1,3-dipolar addition reaction of trimethylsilylacetylene to the azido function of (*R,S*)-**7** in toluene at elevated temperature afforded two products with markedly different chromatographical properties, allowing straightforward separation by column chromatography. Both compounds showed the characteristics of the

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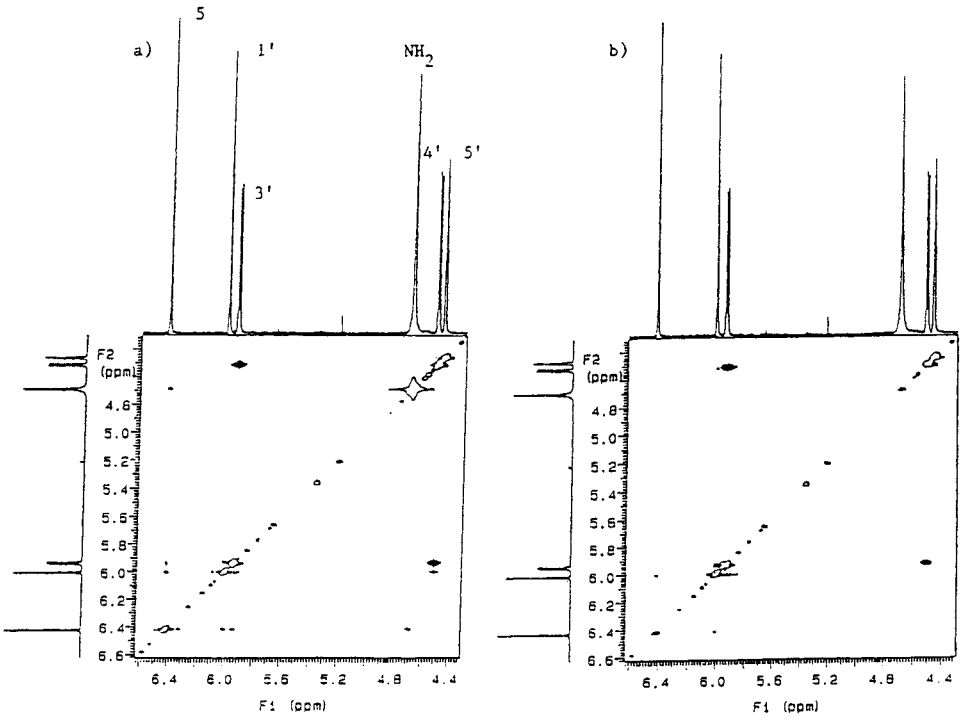

Figure 1a represents a classical NOESY spectrum of compound (*Z*)-6. Several cross peaks are found for H-5, H-1'/3' and H-4' which obscure true NOE peaks and may cause incorrect assignments. Figure 1b shows a QUIET-NOESY spectrum with a selective inversion pulse at δ 6.43 and δ 4.69. True NOE crosspeaks are seen between H-1' and H-3', between H-1' and H-4', and between H-1' and H-5 of the base moiety.

expected silylated 1,2,3-triazoles **8**. Examination of the NMR spectra clearly indicated that both compounds had the β configuration. In particular, the ^{13}C NMR spectra of both isomers showed signals due to the isopropylidene methyl carbons at δ 25.48 and 27.33 and δ 25.47 and 27.36, respectively, in the range (25.5 ± 0.2 and 27.5 ± 0.2)[7] typical for the β-configuration.

Also, the $J_{3',4'}$ values of 4.1 and 4.3 Hz are indicative for a β-configuration of both products (the 2,3-*O*-isopropylidene-α-D-ribofuranosyl-*C*-glycosides have coupling constants of 0-1 Hz, while the β-anomers show values of 1.5-4.5 Hz)[8]. The values of the vicinal coupling constants between the methine CH and C-1', which are moreover also very similar for the two isomers (7.8 and 7.1 Hz respectively), did not allow structural discrimination. In fact there are no reference

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cases for the interpretation of the couplings in this case, since the conformational preferences around the CH-C-1' bond are unknown due to lack of the familiar anomeric effect in these molecules. Strong NOE contacts between the triazole hydrogen and *H*-C(1') in the *S*- or the methine CH in the *R*-epimer are indicative for C(4) substitution of the triazole moiety. Also, additional NOE effects observed in both epimers can only be rationalized if the Me_3Si-group is located at C(4). In similar reactions with unsymmetrical acetylenes, a very bulky group (such as a trimethylsilyl) also tends to occupy selectively the 4-position.[9,10,11] Therefore, it was concluded that both compounds differed only in configuration at the methine carbon. The assignment of both compounds as epimers at this C-bridge could be confirmed from the identification after desilylation.

Epimerization (methine CH) of both isolated compounds [(*R*)-**8** and (*S*)-**8**] on silica gel (when no TEA was added to the eluent) is noteworthy. Individual protodesilylation of (*R*)-**8** and (*S*)-**8** with ammonium fluoride in methanol afforded the epimers (*R*)-**9** and (*S*)-**9**, respectively. The faster eluting desilylated isomer was identified as (*S*)-**9** by X-ray crystallography. As epimerization during the desilylation is unlikely, the less polar isomer after the cycloaddition reaction was assigned as (*S*)-**8**. An attempt to synthesize (*R,S*)-**9** directly by cyclocondensation of (*R,S*)-**7** with ethyl vinyl ether[11] in a pressure vial failed. Deprotection of (*R*)- and (*S*)-**9** is in progress.

In summary, starting from synthon (*R,S*)-**7** we synthesized the fully charactarized acidic labile (*R*)- and (*S*)-**9**, which are first examples of a new series of nucleoside analogues (split homo-*C*-nucleosides).

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EXPERIMENTAL PART

Structure Determination of (*S*)-9 by X-ray Crystallography

(*S*)-**9**: $C_{34}H_{34}N_6O_4$·MeOH, M_r = 622.72; monoclinic, $P2_1$; a = 9.3419(4) Å, b = 13.0077(6) Å, β = 104.723(4)°, c = 14.2666(6) Å, V = 1676.71(13) $Å^3$, Z = 2, D_c = 1.233 Mg m^{-3}, D_x = 1.239 Mg m^{-3}; graphite monochromated Cu Kα radiation, λ = 1.54178 Å; 4265 observed reflections [$I > 2\sigma(I)$], 4480 independent reflections[R(int) = 0.0240]; μ = 0.683 mm^{-1}, F(000) = 652, T = 293(2) K, final R = 0.0423 [$I > 2\sigma(I)$], $\Delta\rho_{max}$ = 0.314 e $Å^{-3}$, $\Delta\rho_{min}$ = -0.135 e $Å^{-3}$; structure solution using SIR92,[12] structure refinement using SHELXL93.[13] An ORTEP stereoview of (*S*)-**9** with the atomic numbering scheme is shown in FIG. 2.

Synthesis

General. Ultraviolet spectra were recorded in MeOH with Schimadzu 2100 UV/vis recording spectrophotometer. The 1D ^1H NMR spectra (about 25 mg in $CDCl_3$) were obtained with a

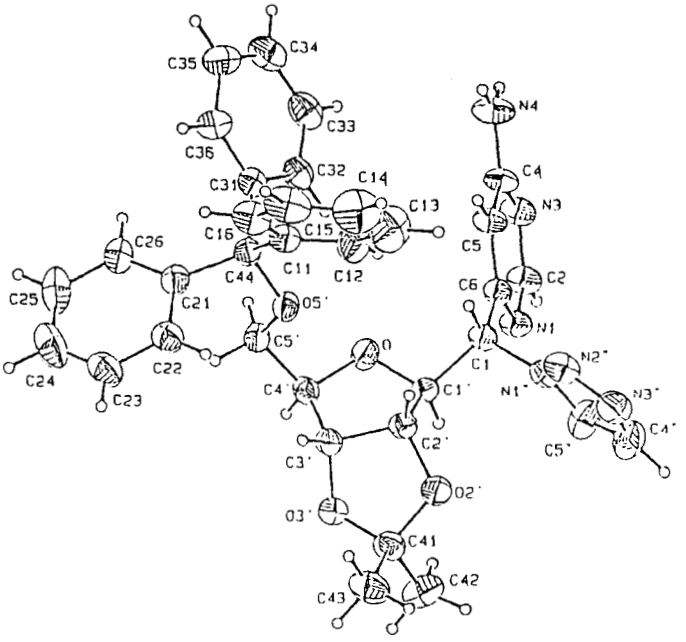

FIG. 2. X-ray structure of (*S*)-9

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Bruker WH 360 spectrometer (University of Ghent), using the residual $CHCl_3$ signal at 7.26 ppm as secondary reference. The homo- and heteronuclear 1D- and 2D-experiments on compounds (*E*)-6 and (*Z*)-6 were performed with a Varian Gemini 200 spectrometer (University of Leuven), with the C resonance of $CDCl_3$ set as ^{13}C reference at 76.89 ppm vs. TMS. For the COSY45 experiment, an acquisition time of 0.324 s, 16 scans, 1K data points and a delay of 3s was used. For the HETCOR experiments, optimised for $^{1}J_{C,H}$ = 140 Hz or for $^{n}J_{C,H}$ = 8 Hz, an acquisition time of 0.071s was used, 400 scans, 1Kx0,5K data points and a relaxation delay of 0.6s. The NOESY and QUIET NOESY experiments were run on a Varian UNITY-500 spectrometer (University of Leuven) the latter operating at 499.693 MHz for proton observation (Software version vnmr 5.1). The experiment was performed in a 5 mm "inverse" detection probe. 90° pulses were 7.1 μs for both experiments (at a transmitter power of 59 dB). A mixing time of 100 ms was used. No zerofilling, 8 scans, 8 dummy scans and 256 increments were used. For the inversion pulses in the QUIET NOESY experiment, i-SNOB-3 pulses were used at offsets 1059.6 Hz and 195.3 Hz from the transmitter frequency (-307.8 Hz) for quiet regions of 100 Hz. Liquid secondary-ion high-resolution mass spectra [HRMS (LSIMS)] were obtained using a Kratos

concept 1H mass spectrometer. Precoated Merck silica gel F_{254} plates were used for TLC, and the spots were examined with UV light at 254 nm and sulfuric acid-anisaldehyde spray. Column chromatography was performed on SÜD-Chemie silica gel (0.2-0.05 mm). Anhydrous solvents were obtained as follows: toluene was refluxed overnight on sodium and distilled; MeOH was obtained by distillation after refluxing overnight on CaH_2.

4-Amino-6-[(*R*- and *S*)-chloro-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-methyl] pyrimidine (*R*)- and (*S*)-(5). Compounds (*R,S*)-**3** (1.55 g, 2.7 mmol) were dissolved in dioxane (100 mL) saturated with ammonia, and the solution was introduced into a sealed tube and heated to 110 °C for 36 h. The solvent was evaporated under reduced pressure, the residue was dissolved in a little EtOAc and subjected to column chromatography. Elution with hexane-EtOAc (1:5) gave the title compounds as a white foam (961 mg, 64%).

MS (LSIMS, thioglycerol) *m/z* 580 $(M + Na)^+$, 336 $(M + Na - CPh_3)^+$, 243 $(CPh_3)^+$. UV and NMR data analogously to ref 3.

(*E*)- and (*Z*)-4-Amino-6-(2',5'-anhydro-1'-deoxy-3',4'-*O*-isopropylidene-6'-*O*-trityl-D-*ribo*-hex-1'-enitol-1'-yl)pyrimidine (*E*)-and (*Z*)-(6). Compounds (*R,S*)-**5** (800 mg, 1.43 mmol) and imidazolylsodium (600 mg, 6.7 mmol) were gently heated (70–80 °C) in DMF (30 mL) overnight. The mixture was diluted with 100 mL of H_2O and extracted twice with 100 mL of Et_2O. The combined organic layer was dried ($MgSO_4$) and evaporated. The obtained residue was purified by column chromatography (EtOAc–hexane, 1:1, and then 2:1) to afford 220 mg of (*E*)-**6** (29 %), 231 mg of (*Z*)-**6** (31 %) both as white solids, together with 70 mg (9 %) of the unresolved mixture (*E,Z*)-**6**.

(*E*)-**6**: UV (MeOH): λ_{max} 270 nm (log ε 4.24); ^{1}H-NMR ($CDCl_3$): δ 1.39 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 3.06 (dd, 2.5, –10.5, H-6B'), 3.58 (dd, 2.5, –10.5, H-6A'), 4.67 (app. d, 6.0, H-4'), 4.78 (app. t, 2.5, H-5'), 4.83 (br s, 2H, NH_2), 5.43 (d, 5.5, H-3'), 5.73 (d, 0.9, H-1'), 7.14 (d, 1.1, pyrim. H-5), 7.20-7.35 (m, 15H, trityl), 8.53 (d, 1.1, pyrim. H-2); ^{13}C-NMR ($CDCl_3$): δ 25.93, 27.06 (2 CH_3), 64.38 (C-6'), 79.38 (C-4'), 82.09 (C-3'), 87.35 (Ph_3C-O), 87.61 (C-5'), 100.91 (C-1'), 102.45 (pyrim. C-5), 112. 97 [$C(CH_3)_2$], 127.16 (Tr_p), 127.86 (Tr_o), 128.43 (Tr_m), 143.08(Tr_i), 158.34 (pyrim. C-2), 161.04 (pyrim. C-4), 162.93 (pyrim. C-6), 163.73 (C-2'); MS (LSIMS, thioglycerol) *m/z* 544 $(M + Na)^+$, 522 $(M + H)^+$, 243 $(trityl)^+$.

(*Z*)-**6**: UV (MeOH): λ_{max} 271 nm (log ε 4.22), 230 nm (log ε 4.33); ^{1}H-NMR ($CDCl_3$): δ 1.35 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.90 (dd, 2.0, –10.5, H-6B'), 3.51 (dd, 2.6, –10.3, H-6A'), 4.46 (d, 2, H-5'), 4.51 (d, 6.2, H-4'), 4.69 (br s, 2H, NH_2), 5.93 (dd, 1, 6.2, H-3'), 6.01 (br s, H-1'), 6.43 (d, 0.8, pyrim. H-5), 7.11-7.29 (m, 15H, trityl), 8.52 (d, 1.1, pyrim. H-2); ^{13}C-NMR

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($CDCl_3$): δ 25.79, 26.72 (2 CH_3), 64.21 (C-6'), 79.63 (C-4'), 81.16 (C-3'), 87.39 (C-5'), 85.30 (CPh_3), 101.57 (C-1'), 102.46 (pyrim. C-5), 112. 23 [$C(CH_3)_2$], 127.00 (Tr_p), 127.79 (Tr_o), 128.41 (Tr_m), 143.19(Tr_i), 158.22 (pyrim. C-2), 161.76 (pyrim. C-4), 162.81 (pyrim. C-6), 165.62 (C-2'); MS (LSIMS, thioglycerol) *m/z* 522 $(M + H)^+$, 243 $(trityl)^+$.

4-Amino-6-[(*R*- and *S*)-(4-trimethylsilyl-1,2,3-triazol-1-yl)-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)methyl]pyrimidine (*R*)- and (*S*)-(8). A solution of 550 mg (0.97 mmol) of **(*R*,*S*)-7** and 1 mL (7.1 mmol) of trimethylsilyl acetylene in 10 mL of dry toluene was heated in a sealed tube for 64 h. At that time TLC revealed the presence of 2 products: one with slightly higher Rf than **(*R*,*S*)-7**, and a more polar one. The reaction mixture was evaporated and purified by column chromatography [hexane- ethyl acetate-TEA, 1. (66:33:1); 2. (50:50:1)]. Two products were isolated: 247 mg (38%) of **(*S*)-8** and 159 mg (30%) of **(*R*)-8** as white foams.

(*S*)-8: UV (MeOH): λ_{max} 232 nm (log ε 4.32), λ_{min} 257 nm (log ε 3.48); ^{1}H-NMR ($CDCl_3$) δ 1.26 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.09 (dd, 4.1, –10.3, H-5B'), 3.29 (dd, 3.2, –10.3, H-5A'), 4.19 (dd, app. q, H-4'), 4.65 (dd, 4.3, 6.4, H-3'), 4.69 (br s, 2H, NH_2), 4.84 (dd, 3.5, 6.4, H-2'), 4.93 (dd, 3.5, 7.8, H-1'), 5.86 (d, 7.8, C-1'-C*H*), 6.04 (s, pyrim. H-5), 7.2-7.4 (m, 15H, trityl), 8.00 (s, triaz. H-5), 8.58 (s, pyrim. H-2); HRMS (LSIMS) *m/z* 663.3116 [MH^+ ($C_{37}H_{43}N_6O_4Si$) = 663.3115]. Elem. anal. calcd. for $C_{37}H_{42}N_6O_4Si$: C: 67.04, H: 6.39, N: 12.68; found C: 66.82, H: 6.41, N: 12.42. **(*R*)-8**: UV (MeOH): λ_{max} 232 nm (log ε 4.33), λ_{min} 257 nm (log ε 3.50), 225 nm (log ε 4.31); ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 3.19 (app. d, 2H, H-5'), 4.21 (dd, app. q, H-4'), 4.41 (dd, 4.1, 6.5, H-3'), 4.63 (dd, 4.2, 6.5, H-2'), 5.00 (dd, 4.2, 7.1, H-1'), 5.10 (br s, 2H, NH_2), 5.87 (d, 7.1, C-1'-C*H*), 6.38 (s, pyrim. H-5), 7.2-7.4 (m, 15H, trityl), 7.73 (s, triaz. H-5), 8.58 (s, pyrim. H-2); HRMS (LSIMS) *m/z* 685.2919 [MNa^+ ($C_{37}H_{42}N_6O_4SiNa$) = 685.2935]; Elem. anal. calcd. for $C_{37}H_{42}N_6O_4Si$: C: 67.04, H: 6.39, N: 12.68; found C: 66.74, H: 6.17, N: 12.56.

The resonances of the protonated C-atoms of (*R*)-**8** were assigned by a (^{13}C, ^{1}H inverse) Heteronuclear Single Quantum Coherence (HSQC) experiment. The spectra of the other analogues were interpreted by analogy with that of (*R*)-**8**.

4-Amino-6-[(*S*)-(1,2,3-triazol-1-yl)-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-methyl]pyrimidine (*S*)-(9). A solution of 100 mg (151 mmol) of (*S*)-**8** in 10 mL of MeOH containing 0.8 mL of a 0.5 N of a methanolic ammonium fluoride solution was kept at 40 °C overnight. TLC analysis revealed almost complete disappearance of all starting material. The solvent was evaporated and the mixture purified by column chromatography (hexane-ethyl acetate-TEA, 50:50:1) to yield 78 mg (88%) of (*S*)-**9** as a white foam. Crystals of (*S*)-**9** for X-ray studies

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TABLE 1. ^{13}C NMR Chemical Shifts of Products **8** and **9**

cmpd	C1'–*C*H	C-1'	C-2'	C-3'	C-4'	C-5'	pyrim C-2	pyrim C-4	pyrim C-5	pyrim C-6	triaz C-4
(*S*)-**8**	65.50	84.69	81.29	82.46	84.53	63.71	158.59	162.19	104.69	162.89	152.07
(*R*)-**8**	66.39	84.43	81.70	81.87	83.97	64.31	158.62	162.02	103.63	163.22	146.11
(*S*)-**9**	65.93	84.69	81.43	82.48	84.69	63.64	158.69	161.82	104.66	162.98	133.91
(*R*)-**9**	65.93	83.99	80.95	81.22	83.78	63.05	158.60	162.44	102.65	163.28	133.87

cmpd	triaz C-5	Me (Ip)	Me (Ip)	C(Ip)	Tr*i*	Tr*m*	Tr*o*	Tr*p*	*C*-Ph3	SiMe3
(*S*)-**8**	129.07	25.47	27.36	114.03	143.52	128.66	127.78	127.06	86.72	- 1.24
(*R*)-**8**	129.63	25.48	27.33	114.28	143.47	128.64	127.79	127.04	86.87	- 1.23
(*S*)-**9**	123.78	25.42	27.32	114.15	143.47	128.66	127.82	127.10	86.77	-
(*R*)-**9**	124.77	25.44	27.31	114.84	143.31	128.69	127.79	127.15	86.97	-

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were obtained from MeOH. UV (MeOH): λ_{max} 232 nm (log ε 4.28), λ_{min} 224 nm (log ε 4.27); ^{1}H-NMR ($CDCl_3$) δ 1.26 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.11 (dd, 4.0, –10.3, H-5B'), 3.30 (dd, 3.2, –10.3, H-5A'), 4.21 (dd, app. q, H-4'), 4.69 (dd, 4.0, 6.4, H-3'), 4.82 (dd, 3.6, 6.4, H-2'), 4.87 (br s, NH_2), 4.91 (dd, 3.6, 8.1, H-1'), 5.82 (d, 8.1, C-1'-C*H*), 6.08 (s, pyrim. H-5), 7.22-7.42 (m, 15H, trityl), 7.72 (s, triaz. H-4), 8.08 (s, triaz. H-5), 8.56 (s, pyrim. H-2); HRMS (LSIMS) *m/z* 613.2524 [MNa^+ ($C_{34}H_{34}N_6O_4Na$) = 613.2539]; Elem. anal. calcd. for $C_{34}H_{34}N_6O_4$: C: 69.13, H: 5.80, N: 14.23; found C: 69.03, H: 5.81, N: 14.08.

4-Amino-6-[(*R*)-(1,2,3-triazol-1-yl)-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-methyl]pyrimidine (*R*)-(9). Removal of the trimethylsilyl group of (*R*)-**8** was performed as for (*S*)-**8** giving (*R*)-**9** as a white foam with similar yield. UV (MeOH): λ_{max} 232 nm (log ε 4.30), λ_{min} 256 nm (log ε 3.46), 226 nm (log ε 4.29); ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 3.22 (dd, 3.7, –10.5, H-5B'), 3.37 (dd, 3.1, –10.5, H-5A'), 4.11 (dd, app. q, H-4'), 4.48 (dd, 4.6, 6.8, H-3'), 4.59 (dd, 4.6, 6.8, H-2'), 4.99 (dd, app. t, 4.9, H-1'), 5.06 (br s, 2H, NH_2), 6.01 (d, 4.9, C-1'-C*H*), 6.02 (br s, pyrim. H-5), 7.22-7.42 (m, 15H, trityl), 7.54 (d, 0.5, triaz. H-4), 8.04 (d, 0.9, triaz. H-5), 8.58 (d, 0.5, pyrim. H-2); HRMS (LSIMS) *m/z* 613.2530 [MNa^+

($C_{34}H_{34}N_6O_4Na$) = 613.2539]; Elem. anal. calcd. for $C_{34}H_{34}N_6O_4$: C: 69.13, H: 5.80, N: 14.23; found C: 68.85, H: 5.62, N: 14.07.

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