Oligonucleosides with a Nucleobase-Including Backbone

Part 2

Synthesis and Structure Determination of Adenosine-Derived Monomers

by **Hiroki Gunji** and **Andrea Vasella***

Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich

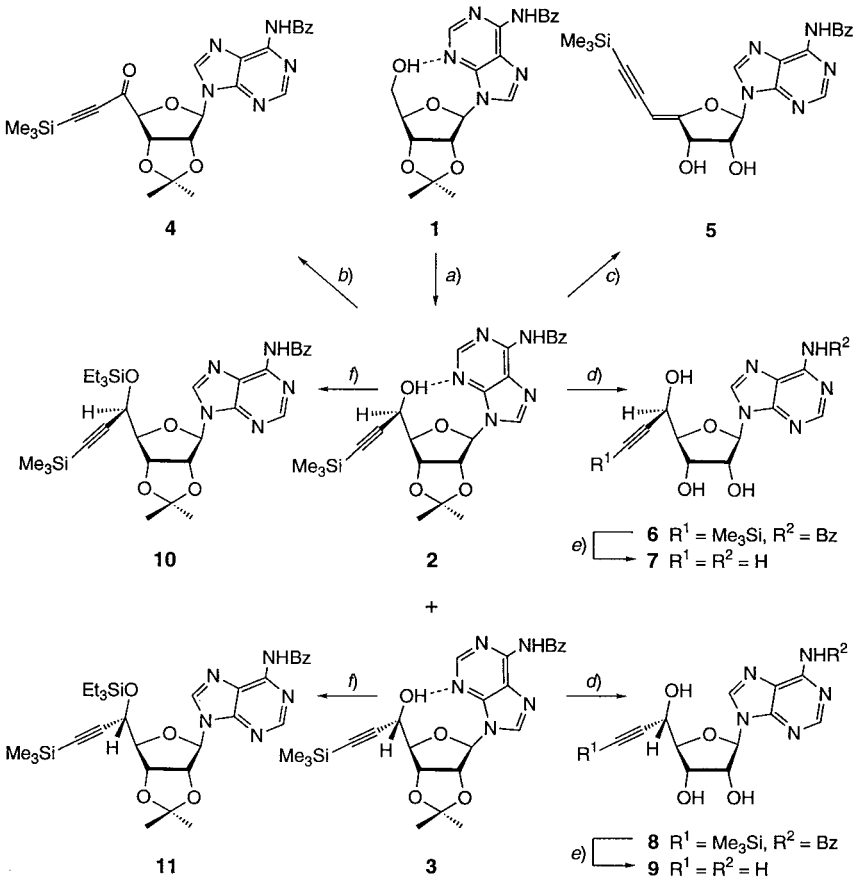
The synthesis and structure determination of adenosine-derived monomeric building blocks for new oligonucleosides are described. Addition of Me_3Si-acetylide to the aldehyde derived from the known partially protected adenosine **1** led to the epimeric propargylic alcohols **2** and **3**, which were oxidised to the same ketone **4**, while silylation and deprotection led to **7** and **9** (*Scheme 1*). Introduction of an I substituent at C(8) of the propargylic silyl ethers **10** and **11** was not satisfactory. The protected adenosine **12** was, therefore, transformed in high yield into the 8-chloro derivative **13** by deprotonation and treatment with $PhSO_2Cl$; the iodide **15** was obtained in a similar way (*Scheme 2*). The 8-Cl and the 8-I derivatives **13** and **15** were transformed into the propargylic alcohols **17**, **18**, **25**, and **26**, respectively (*Scheme 3*). The propargylic derivatives **2**, **10**, **17**, **19**, **23**, **25**, and **27** were correlated, and their (5′*R*) configuration was determined on the basis of NOEs of the anhydro nucleoside **19**; similarly, correlation of **3**, **11**, **18**, **20**, **24**, **26**, and **28**, and NOE's of **20** evidenced their (5′*S*)-configuration.

Introduction. – In the preceding paper [1], we have described the design of a new class of oligonucleotide analogues, and the synthesis of uridine-derived monomers and dimers. We now report the synthesis of the analogous adenosine derivatives by addition of Me_3Si-acetylide to the aldehyde derived from N^6-benzoyl-2′,3′-O-isopropylidene-adenosine [2], leading to a mixture of diastereoisomeric propargyl alcohols, the introduction of a halo substituent at C(8) as it is required for the projected cross-coupling, and the determination of the configuration of these products.

Results and Discussion. – The known partially protected adenosine **1** [2] was oxidised by the *Pfitzner-Moffatt* method [3][4], and the resulting labile aldehyde was directly treated with Me_3Si-ethynylmagnesium bromide in THF at 0° to yield *ca.* 40–45% of a 1:1 mixture of the epimeric propargylic alcohols (*Scheme 1*). These were readily separated by flash chromatography (FC) to afford **2** and **3**, each in *ca.* 20% yield from **1**. *Dess-Martin* oxidation [5] transformed both alcohols into the same ketone **4**, confirming that **2** and **3** are epimeric at C(5′).

Deprotection of **2** and **3** required mild conditions. Treatment of **2** with 1N aqueous HCl at 25° with 50% aqueous $Cl_2CHCOOH$ at 60°, or with 50% AcOH at 40°, not only cleaved the 1,3-dioxolane ring, but also caused dehydration, leading to the enyne **5**. The (*Z*)-configuration of **5** is indicated by the upfield shift of H–C(5′) at 4.71 ppm (4.80 ppm is a typical value for such (*Z*)-enynol ethers, whereas the corresponding (*E*)-enynol ethers resonate at 5.2–5.4 ppm [6][7]). Milder conditions (5 mol-% of camphorsulfonic acid in MeOH at 25° or in 75% AcOH at 25°) did not affect **2**.

Scheme 1



a) *N,N'*-Dicyclohexylcarbodiimide (DCC), $Cl_2CHCOOH$, DMSO; $Me_3Si-C{\equiv}CMgBr$, THF; **2** (21%) and **3** (20%). *b*) *Dess-Martin* periodinane, CH_2Cl_2; 94%. *c*) $Cl_2CHCOOH/H_2O$ 1:1; 80%. *d*) 80% aq. HCOOH; **6** (74%), **8** (64%). *e*) 25% aq. NH_4OH, MeOH; **7** (86%), **9** (96%). *f*) Et_3SiCl, imidazole, DMF; **10** (84%), **11** (58%).

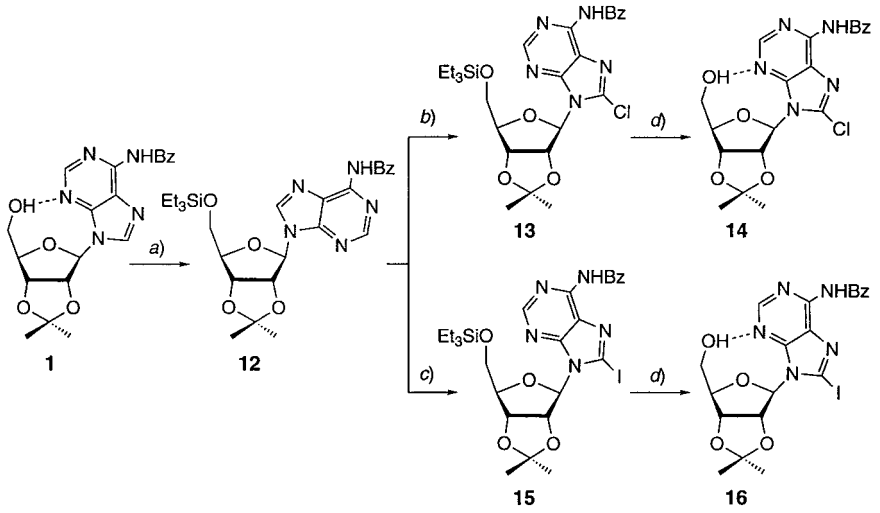
Deisopropylidenation of **2** without dehydration was, however, accomplished with 80% HCOOH at room temperature for 8 h, to yield 74% of the triol **6**. The fully deprotected propargylic alcohol **7** was prepared in 86% by hydrolysis of **6** with aqueous NH_4OH. In the same way, we obtained the epimer **9** *via* **8** in an overall yield of 61% from **3**.

Exploratory experiments to introduce an I substituent at C(8), required for cross-coupling of the monomer, were performed with the propargylic triethylsilyl ether **10** that was readily available in 84% from **2**. Similarly, silylation of **3** afforded **11** (58%). Unfortunately, yields of the attempted iodination of **10** were not satisfactory (*cf.* below), so that we introduced the halogen substituent before the alkynyl group.

8-Chloroadenosine derivatives have been prepared by several methods in yields of 10–63% with HCl and *m*-chloroperbenzoic acid (MCPBA) [8], *N*-chlorosuccinimide (NCS) [9][10], NCS and MCPBA [11], *t*-butyl hypochlorite [12], or Bu_4NICl_4 [13].

Recently, excellent yields were obtained by lithiation (lithium diisopropylamide (LDA)) followed by chlorination with C_2Cl_6 [14]. As a 2-chloroimidazole derivative had been prepared by deprotonation of *N*-tritylimidazole with LDA followed by treatment with TsCl [15], we have independently studied the analogous chlorination of **12**, readily available in high yields by silylation of **1** (*Scheme 2*), but substituting TsCl with $PhSO_2Cl$, to avoid competitive deprotonation of the reagent. Regioselective lithiation of **12** with LDA at $-78°$ for 3 h in THF [16], followed by treatment with $PhSO_2Cl$ gave the 8-Cl derivative **13** in 97%[1]). Formation of the chloride was confirmed by its mass spectrum, the peaks at *m*/*z* 560 and 562 appearing in a 3 : 1 ratio. Treating the anion resulting from **12** with I_2 [17] afforded the 8-I derivative **15** in an excellent yield. Desilylation of **13** and **15** with $Bu_4NF \cdot 3H_2O$ (TBAF) in THF gave quantitatively the halo alcohols **14** and **16**, respectively.

Scheme 2



a) Et_3SiCl, imidazole, DMF; 97%. *b*) LDA, THF, then $PhSO_2Cl$; 97%. *c*) LDA, THF, then I_2; 91%. *e*) TBAF · $3H_2O$, THF; **14** (94%), **16** (100%).

To transform the chloro alcohol **14** into the propargylic alcohols **17** and **18** (*Scheme 3*), we proceeded similarly as described for the synthesis of **2** and **3**. *Pfitzner-Moffatt* oxidation of **14**, followed by addition of Me_3Si-ethynylmagnesium bromide in THF at 0° and chromatographic separation of the products gave **17** (16%) and **18** (17%). Their treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene at 50° led to the anhydronucleosides **19** and **20**, respectively, while NaH, as originally used for the synthesis of an 8,5′-anhydroadenosine [18] from 8-bromo-2′,3′-*O*-isopropylideneadenosine, led to degradation (*cf.* [19]), presumably by initiating cleavage of the C(5′)-ethynyl bond.

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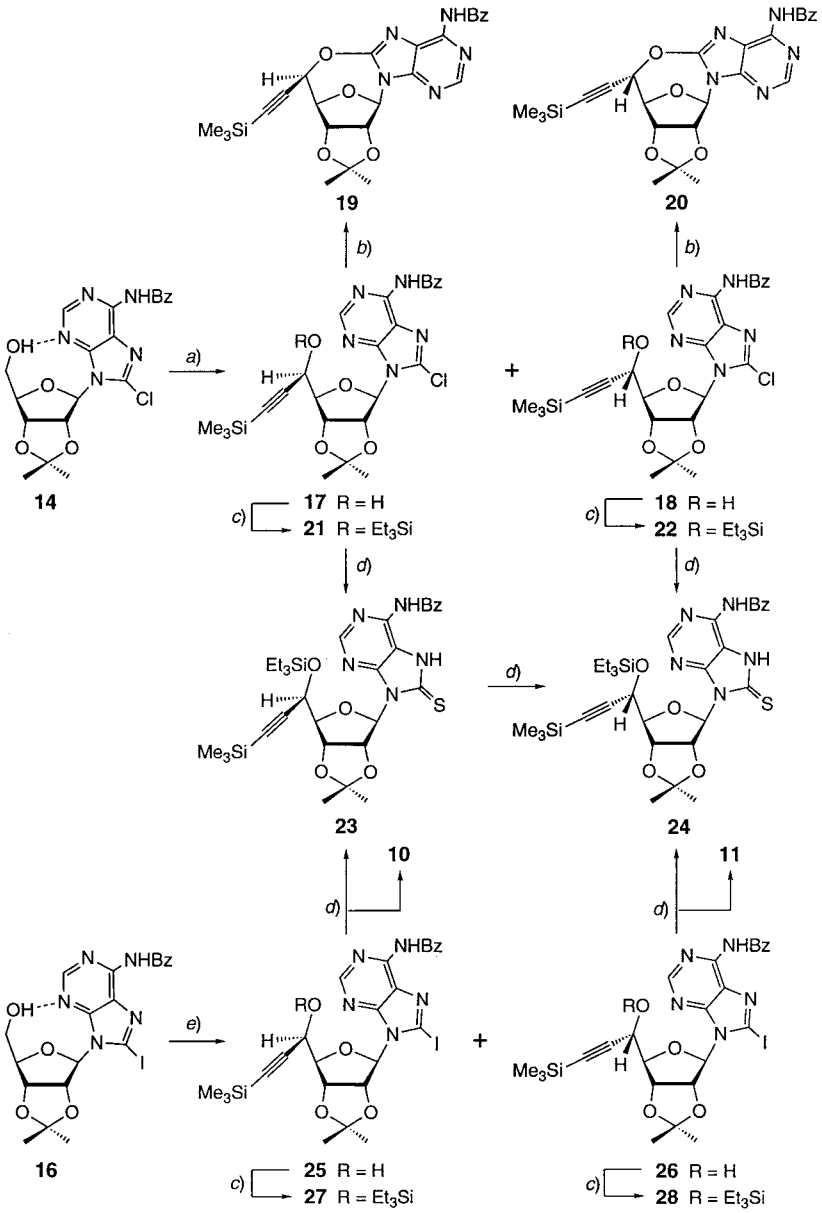
[1]) $PhSO_2Cl$ is cheaper and less toxic than C_2Cl_6, and may well prove the reagent of choice for this chlorination.

Scheme 3



a) DCC, $Cl_2CHCOOH$, DMSO; $Me_3Si-C\equiv CMgBr$, THF; **17** (16%), **17**/**18** (9%), and **18** (17%). *b*) DBU, toluene; **19** (76%); **20** (67%). *c*) Et_3SiCl, imidazole, DMF; **21** (72%); **22** (73%); **27** (10% from **16**); **28** (8% from **16**). *d*) *N*-Phenylthiourea, toluene; **23** (98%); **24** (82%). *e*) DCC, $Cl_2CHCOOH$, DMSO; $Me_3Si-C\equiv CMgBr$, THF, then I_2; **25** (19%) and **26** (20%). *f*) Thiourea, toluene; **10** (26%) and **23** (61%); **11** (38%) and **24** (53%).

Molecular modeling[2]) confirmed the expected rigidity of the azadioxa[4.2.1]nonane skeleton of **19** and **20**. The furanose ring of **19** and **20** adopts a E_O conformation as evidenced by $J(1',2') = J(3',4') = 0$ Hz (cf. *Table 1* in *Exper. Part*). The configuration at C(5′) was determined by NOE experiments. The propargylic H–C(5′) of **20** resonates as a *doublet* at 5.20 ppm ($J(4',5') = 2.3$ Hz). Its irradiation led to a NOE of 7.8% for H–C(3′) at 5.08 ppm, and of 15% for H–C(4′) at 4.73 ppm (*cf.* [19]), evidencing the (5′*S*)-configuration of **20** and, hence, of **18**. Irradiation of the propargylic H–C(5′) of **19** resonating as a *doublet* ($J(4',5') = 0.8$ Hz) at 4.95 ppm led only to a NOE (14%) for H–C(4′) at 4.76 ppm, evidencing the (5′*R*)-configuration of **19** and **17**.

To correlate the configuration of **17** and **18** with that of **10** and **11** (respectively **2** and **3**), we prepared the triethylsilyl ethers **21** and **22** under standard conditions. However, attempts to dechlorinate these derivatives (Bu_3SnH/AIBN) failed. We therefore planned to prepare the iodo derivatives **27** and **28**, and to correlate these with the chlorides **21** and **22**, on the one hand, and with the dehalo compounds **10** and **11**, on the other hand. Towards this goal, we transformed the chlorides **17** and **18** into the thiones **23** and **24**, respectively, by silylation to **21** and **22** followed by treatment with *N*-phenylthiourea in toluene at 60°[3]). The δ(C(8)) values of **23** (165.8 ppm) and **24** (169.9 ppm) evidence the preponderance of the thiourea tautomer (*cf.* [23][24]).

The iodo-propargylic alcohols **25** and **26** were prepared from **16** by oxidation to the corresponding aldehyde, followed by addition of Me_3Si-ethynylmagnesium bromide (*Scheme 3*). The I-substituent at C(8) was exchanged with MgBr during the *Grignard* reaction, and the crude product had to be treated with I_2 to obtain the desired iodides **25** and **26**; FC yielded each one in *ca.* 20%[4]). Addition of H_2O to the crude *Grignard* product gave the de-iodinated alcohols **2** and **3**.

Initially, we attempted to prepare the 8,5′-anhydro nucleosides **19** and **20** from the iodides **25** and **26**. Treating these iodides with DBU under conditions that had proven effective for the cyclisation of the chloro alcohols **17** and **18** led only to *N*-debenzoylation. No cyclisation products were observed, indicating that I is too bulky for an effective nucleophilic attack of the alkoxide.

We therefore transformed the iodo alcohols **25** and **26** into the corresponding 8-thiocarbonyl compounds. The alcohol **25** was protected by triethylsilylation, and the resulting **27** was treated with thiourea [21][22] at 60° in toluene to give a de-iodinated product and the thiourea **23** in 26 and 61% yield, respectively. The de-iodinated product was identified with **10** by comparison with the authentic sample derived from the propargylic alcohol **2** (*Scheme 1*). The thiourea **23** was identical with an authentic sample derived from **17** *via* **21** for which the (*R*)-configuration at C(5′) had been deduced, thus also establishing the (5′*R*)-configuration of **10**.

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[2]) *Macromodel V. 6.0* (AMBER* force field, gas phase) [20].

[3]) Thiourea in EtOH has been used for the analogous transformation of 8-bromoadenosine derivatives [21][22]. We substituted toluene for EtOH to avoid desilylation; *N*-phenylthiourea proved more reactive than thiourea.

[4]) As mentioned above, we have also attempted to iodinate **10**. Deprotonating **10** with LDA at −78° in THF led rapidly to blackening. Addition of I_2 followed by standard workup and chromatography yielded 15% only of slightly impure iodo derivative **27**, reflecting the sensitivity of the acetylene **10** to strongly basic conditions.

Similarly, we prepared the epimeric thiourea **24** (53%) from the epimeric alcohol **26** *via* the iodo-silyl ether **28**; again, the transformation was accompanied by partial deiodination, leading in 38% yield to the silyl ether **11**, establishing the (5′*S*)-configuration.

The $J(1',2')$ values of the secondary alcohols **2**, **3**, **17**, and **18** (*cf. Table 1* in *Exper. Part*), and of the primary alcohols **1**, **14**, and **16** (*cf. Table 2* in *Exper. Part*) are sensibly larger (4.5–5.5 Hz) than the $J(1',2')$ values of the corresponding silyl ethers **10**–**13**, **15**, **21**–**24**, **27**, and **28** (2.0–3.0 Hz, *Tables 1* and *2*). This difference correlates with differences between the $J(3',4')$ values of the alcohols that are small ($\leq$1.5 Hz) and the $J(3',4')$ values of the silyl ethers that are larger (1.5–4.0 Hz), expressing that the alcohols prefer the (*S*)-conformation and the silyl ethers a *ca.* 1:1 (*N*)/(*S*) equilibrium. The $J(4',5')$ values of the alcohols **1**–**3**, **14**, and **16**–**18** are small (1.5–2.5 Hz), indicating a synclinal arrangement of H–C(4′) and H–C(5′) of the allyl alcohols, and of H–C(4′) and both H–C(5′) of the adenosines. The strong downfield shift of the OH signal in $CDCl_3$ (5.57–5.75 ppm for the primary alcohols **1**, **14**, and **16**; 6.06 and 6.21 ppm for the L-*talo*-propargyl alcohols **3** and **18**, 6.91 and 6.86 ppm for the D-*allo*-propargyl alcohols **2** and **17**) evidences the intramolecular O(5′)H···N(3) H-bond, which leads to antiperiplanar H–C(4′) and C(5′)–O(5′) bonds. The δ(HO–C(5′)) values show that propargylic OH groups are more highly acidic than HO–C(5′) of adenosine and, thus, better H-bond donors, as mentioned before [25]. Such intramolecular H-bonds are well-documented (see, *e.g.*, [26–31]). The nine-membered ring formed by the H-bond is rigid [26][27][32], leading to characteristic $J(5',OH)$ values of 0–1.5 Hz for the D-*allo*-propargyl alcohols **2** and **17**, and of 10.5–11.0 Hz for the L-*talo*-propargyl alcohols **3** and **18**. In agreement with the rigid conformation, the $J(5'_{pro\text{-}S},OH)$ values of the adenosines **1**, **14**, and **16** are small (1.5–2.0 Hz) and the $J(5'_{pro\text{-}R},OH)$ values are large (11.0–11.5 Hz). In **2** and **17**, the O–H bond is antiperiplanar to the $Me_3Si-C\equiv C$ substituent and in **3** and **18** *synclinal*; an anisotropy effect of the acetyleno group is responsible for the shielding of HO–C(5′) of **3** and **18** ($\Delta\delta \approx$ 0.7 ppm). The $J(4',5')$ value increases from 3.7–4.3 Hz for the 8-unsubstituted silyl ethers **10**–**12** to 6.0–6.5 Hz for the 8-halogenated silylated ribosides **13** and **15**, and to 7.5–8.0 Hz for the 8-halogenated propargylic silyl ethers **21**–**23**, **27**, and **15**, indicating a preferred *antiperiplanar* orientation of H–C(4′) and H–C(5′) in the 8-halogenated derivatives due to steric interaction with the bulkier nucleobase.

The orientation of the nucleobase has a strong influence on the chemical shift of H–C(1′) and H–C(2′). 8-Unsubstituted adenosines prefer the *anti*-conformation, whereas 8-substituted derivatives prefer the *syn*-conformation, as evidenced by a downfield shift of the H–C(2′) signal [19][32–36]. The *syn*-conformation is also preferred by the alcohols **1**–**3**, **14**, and **16**–**18** on account of the intramolecular H-bond (see also [26][27][29][32]) that directs X–C(8) close to H–C(1′). Indeed, the H–C(1′) signal moves downfield with increasing polarity of the C(8)-substituent (H: 5.94–6.02, I: 6.08, Cl: 6.14–6.21 ppm), whereas H–C(2′) is only weakly influenced (H: 5.15–5.25, I/Cl: 5.32 ppm). The 5′,8-anhydrides **19** and **20** adopt an *anti*-conformation and show the expected upfield shift for H–C(2′), which resonates at 4.80–4.81 ppm. The downfield shift of H–C(1′) appearing at 6.45–6.49 ppm is due to the vicinity of N(3). The 8-unsubstituted silyl ethers **10**–**12** should prefer an *anti*-conformation, and the 8-halogenated silyl ethers **13**, **15**, **21**–**24**, **27**, and **28** a *syn*-conformation. Indeed,

H–C(2′) of **13**, **15**, **21**–**24**, **27**, and **28** appears at lower field (5.60–5.90 ppm) than H–C(2′) of **10**–**12** (5.20–5.26 ppm), evidencing the *syn*-conformation.

De-isopropylidenation shifts the equilibrium strongly to the (*S*)-conformer as indicated by the *J*(1′,2′) values (7.2 for **8** in (D_6)acetone, 7.9 for **9** in CD_3OD, 8.4 for **6** in (D_6)acetone, and 8.6 for **7** in (D_6)DMSO), and increases the ring pucker (sum of *J*(1′,2′) and *J*(3′,4′) varies between 9.1 for **7** and 9.9 for **9**) [37].

We thank Dr. *B. Bernet* for checking the experimental part and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

General. Solvents were distilled before use: THF from Na/benzophenone, CH_2Cl_2 from CaH_2. TLC: *Merck* silica gel *60F-254* plates; detection by heating with anisaldehyde soln. (5.0 ml of anisaldehyde, 6.7 ml of conc. H_2SO_4, 2.0 ml of AcOH, 180 ml of EtOH). Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). M.p.: uncorrected. Optical rotations: 1-dm cell at 25° and 589 nm. UV Spectra: 10-mm cell at 25°. IR Spectra: KBr or 2% $CHCl_3$ soln. ^{1}H (300 MHz, if not indicated otherwise) and ^{13}C-NMR (75 MHz, if not indicated otherwise): chemical shifts δ in ppm and coupling constants *J* in Hz. FAB-MS: 3-nitrobenzyl alcohol, unless indicated otherwise.

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**2**) *and* N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]-adenine* (**3**). At 15°, a soln. of **1** (4.32 g, 10.51 mmol) and DCC (6.50 g, 31.50 mmol) in dry DMSO (24.0 ml) was treated dropwise with $Cl_2CHCOOH$ (0.43 ml, 5.21 mmol), stirred for 10 min, warmed to 25°, stirred for 90 min, and filtered. The residue was washed with small amounts of DMSO, and the combined filtrates were washed with hexane (4 × 150 ml). The DMSO layer was diluted with $CHCl_3$ (650 ml), washed with H_2O (2 × 200 ml), dried (Na_2SO_4), and evaporated. This crude aldehyde was processed as described below.

At 0°, a soln. of EtMgBr (32.0 mmol) in THF (52 ml) was treated dropwise with trimethylsilylacetylene (4.5 ml, 31.8 mmol), stirred for 10 min, warmed to 25°, stirred for 30 min, cooled to 0°, and treated with a soln. of the crude aldehyde in dry THF (129 ml). After stirring for 3 h, the mixture was treated with sat. aq. NH_4Cl soln. (150 ml) and H_2O (30 ml). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 80 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (420 g of silica gel; $CHCl_3$/AcOEt 1:1) gave **2** (1.099 g, 21%) and **3** (1.044 g, 20%).

Data of **2**: Yellow solid. R_f ($CHCl_3$/AcOEt 1:1) 0.45. M.p. 119°. $[\alpha]_D^{25} = -45.4$ (*c* = 1.00, $CHCl_3$). UV ($CHCl_3$): 278.0 (17000). IR ($CHCl_3$): 3402*w*, 3202*w*, 3008*m*, 2180*w*, 1712*m*, 1611*s*, 1590*s*, 1505*m*, 1480*m*, 1457*s*, 1419*m*, 1385*m*, 1360*m*, 1332*m*, 1296*m*, 1252*s*, 1155*m*, 1111*s*, 1089*s*, 1046*m*, 1029*w*, 1003*w*, 971*w*, 957*w*, 894*w*, 849*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.20 (*s*, Me_3Si); 1.41, 1.67 (2*s*, Me_2C); 7.47–7.65 (*m*, 3 arom. H); 7.96–8.05 (*m*, 2 arom. H); 9.12 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.2 (*d*, C(2)); 150.4 (*s*, C(6)); 150.2 (*s*, C(4)); 142.5 (*d*, C(8)); 133.4 (*s*); 133.0 (*d*); 128.9 (2*d*); 127.9 (2*d*); 124.3 (*s*, C(5)); 114.3 (*s*, Me_2C); 101.3 (*s*, C(6′)); 94.7 (*d*, C(1′)); 92.2 (*s*, C(7′)); 87.7 (*d*, C(4′)); 82.5 (*d*, C(2′)); 80.8 (*d*, C(3′)); 63.6 (*d*, C(5′)); 27.7, 25.7 (2*q*, Me_2C); −0.2 (*q*, Me_3Si). FAB-MS: 508 ($[M+1]^+$). Anal. calc. for $C_{25}H_{29}N_5O_5Si \cdot H_2O$ (525.64): C 57.13, H 5.94, N 13.32; found: C 56.83, H 5.74, N 13.01.

Data of **3**: Yellow solid. R_f ($CHCl_3$/AcOEt 1:1) 0.36. M.p. 117–118° (acetone/hexane). $[\alpha]_D^{25} = +20.2$ (*c* = 1.10, $CHCl_3$). UV ($CHCl_3$): 278.0 (16000). IR ($CHCl_3$): 3403*w*, 3269*w*, 3008*m*, 2175*w*, 1710*m*, 1612*s*, 1588*s*, 1506*m*, 1480*m*, 1457*s*, 1419*m*, 1385*m*, 1360*m*, 1330*m*, 1257*s*, 1156*m*, 1119*s*, 1087*s*, 1049*m*, 1030*w*, 1017*w*, 928*w*, 847*s*, 643*w*, 563*w*, 509*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.08 (*s*, Me_3Si); 1.37, 1.63 (2*s*, Me_2C); 7.55–7.64 (*m*, 3 arom. H); 7.96–8.05 (*m*, 2 arom. H); 9.17 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.6 (*s*, C=O); 152.4 (*d*, C(2)); 150.6 (*s*, C(6)); 150.1 (*s*, C(4)); 142.5 (*d*, C(8)); 133.4 (*s*); 132.9 (*d*); 128.9 (2*d*); 127.9 (2*d*); 124.1 (*s*, C(5)); 114.5 (*s*, Me_2C); 102.8 (*s*, C(6′)); 94.0 (*d*, C(1′)); 90.7 (*s*, C(7′)); 87.7 (*d*, C(4′)); 83.1 (*d*, C(2′)); 81.8 (*d*, C(3′)); 63.5 (*d*, C(5′)); 27.5, 25.3 (2*q*, Me_2C); −0.2 (*q*, Me_3Si). FAB-MS: 508 ($[M+1]^+$).

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-β*-D-ribo-*hept-6-ynos-5-ulofuranosyl]-adenine* (**4**). At 25°, a soln. of **2** (24.4 mg, 48.1 μmol) in dry CH_2Cl_2 (0.98 ml) was treated with *Dess-Martin* periodinane [5] (30.0 mg, 70.7 μmol), stirred for 1.5 h, diluted with CH_2Cl_2 (*ca.* 0.5 ml), washed with sat. aq. $NaHCO_3$ soln./sat. aq. $Na_2S_2O_3$ soln. 1:7 (1.0 ml), and extracted with CH_2Cl_2 (0.3 ml). The combined org. layers were dried (Na_2SO_4) and evaporated. FC (0.8 g of silica gel; $CHCl_3$/AcOEt 5:4) gave **4** (22.9 mg, 94%). Yellow

Table 1. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Propargyl Derivatives* **2**–**4**, **10**, **11**, **17**–**24**, **27**, and **28** *in $CDCl_3$ Solution*

	2	**3**	**17**	**18**	**19**	**20**			
H–C(2)	8.75	8.78	8.71	8.80	8.67	8.77			
H–C(8)	8.07	8.13	–	–	–	–			
H–C(1′)	5.94	6.02	6.14	6.21	6.45	6.49			
H–C(2′)	5.15	5.19	5.20	5.25	4.80	4.81			
H–C(3′)	5.20	5.01	5.17	5.02	5.26	5.08			
H–C(4′)	4.57	4.54	4.54	4.56	4.76	4.73			
H–C(5′)	4.73	4.63	4.73	4.64	4.95	5.20			
HO–C(5)	6.91	6.06	6.86	6.21	–	–			
J(1′,2′)	5.0	4.5	5.0	5.0	0	0			
J(2′,3′)	6.0	5.8	5.0	6.0	5.5	5.5			
J(3′,4′)	< 0.5	1.4	< 0.5	1.5	0	0			
J(4′,5′)	1.5	2.2	2.0	2.5	0.8	2.3			
J(5′,OH)	1.5	10.5	0	11.0	–	–			
	4	**10**	**11**	**21**	**22**	**23**	**24**	**27**	**28**
H–C(2)	8.72	8.85	8.87	8.77	8.80	8.41	8.45	8.73	8.76
H–C(8)	8.18	8.23	8.45	–	–	–	–	–	–
H–C(1′)	6.33	6.25	6.27	6.24	6.25	6.81	6.81	6.13	6.15
H–C(2′)	5.58	5.20	5.20	5.85	5.73	5.60	5.59	5.90	5.77
H–C(3′)	5.81	5.05	4.92	5.24	5.26	5.21	5.19	5.26	5.29
H–C(4′)	4.79	4.45	4.49	4.22	4.26	4.22	4.21	4.22	4.22
H–C(5′)	–	4.60	4.57	4.43	4.46	4.63	4.68	4.41	4.41
J(1′,2′)	< 0.5	3.0	2.8	2.0	2.5	2.5	2.5	2.0	2.0
J(2′,3′)	6.5	6.0	6.0	6.3	6.5	6.5	6.5	6.0	6.5
J(3′,4′)	1.0	2.0	1.5	2.8	3.5	4.0	4.0	2.8	3.0
J(4′,5′)	–	4.3	4.0	7.5	8.0	8.0	7.8	8.0	8.0

solid. R_f ($CHCl_3$/AcOEt 5:4) 0.44. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 1*; additionally, 0.12 (*s*, Me_3Si); 1.45, 1.67 (2*s*, Me_2C); 7.53–7.69 (*m*, 3 arom. H); 7.98–8.10 (*m*, 2 arom. H); 8.98 (br. *s*, NH).

N^6-*Benzoyl-9-[(Z)-5,6,7-trideoxy-7*-C-*(trimethylsilyl)-β*-D-erythro-*hept-4-en-6-ynofuranosyl]adenine* (**5**). At 25°, a soln. of **2** (36.3 mg, 71.5 μmol) in 50% aq. $Cl_2CHCOOH$ (1.8 ml) was stirred at 60° for 2 h, diluted with $CHCl_3$ (10 ml), washed with H_2O (5 ml) and brine (3 ml), dried (Na_2SO_4), and evaporated. FC (1.5 g of silica gel; $CHCl_3$/acetone 1:1) gave **5** (25.2 mg, 80%). White solid. R_f ($CHCl_3$/acetone 1:1) 0.42. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.22 (*s*, Me_3Si); 4.39 (*d*, J = 2.0, HO–C(2′)); 4.61 (*dd*, J = 5.5, 2.0, H–C(2′)); 4.71 (*d*, J = 1.0, H–C(5′)); 4.97 (br. *dd*, J = 5.9, 5.5, H–C(3′)); 5.93 (*s*, H–C(1′)); 6.02 (*d*, J = 5.9, HO–C(3′)); 7.38–7.87 (*m*, 3 arom. H); 7.97–8.04 (*m*, 2 arom. H); 8.39 (*s*, H–C(8)); 8.53 (*s*, H–C(2)); 8.54 (br. *s*, NH).

N^6-*Benzoyl-9-[6,7-dideoxy-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**6**). At 25°, a soln. of **2** (32.7 mg, 64.4 μmol) in 80% aq. HCOOH (1.6 ml) was stirred for 8 h. The mixture was evaporated and co-evaporated several times with PhMe. FC (1.5 g of silica gel; $CHCl_3$/acetone 2:3) gave **6** (22.3 mg, 74%). White solid. R_f ($CHCl_3$/acetone 2:3) 0.50. M.p. 184°. $[\alpha]_D^{25} = -102.4$ (c = 1.01, acetone). UV (MeOH): 276.0 (16000), 230.0 (12000). IR (KBr): 3322*m*, 2957*w*, 2177*w*, 1704*m*, 1612*s*, 1585*s*, 1514*m*, 1486*m*, 1455*s*, 1411*m*, 1332*m*, 1252*s*, 1121*m*, 1073*s*, 955*m*, 845*s*, 798*m*, 760*m*. ^{1}H-NMR (300 MHz, (D_6)acetone): 0.20 (*s*, Me_3Si); 4.23 (*dd*, J = 3.1, 1.3, H–C(4′)); 4.49 (br. *d*, addn. of D_2O → *dd*, J = 5.5, 1.3, H–C(3′)); 4.56 (br. *s*, exchanged with D_2O, OH); 4.69 (*t*, J = 3.1, H–C(5′)); 4.92–5.03 (*m*, addn. of D_2O → 4.90, *dd*, J = 8.4, 5.5, H–C(2′)); 5.32 (br. *s*, exchanged with D_2O, OH); 6.10 (*d*, J = 8.4, H–C(1′)); 6.31 (*d*, J = 3.1, exchanged with D_2O, HO–C(5′)); 7.51–7.68 (*m*, 3 arom. H); 8.11–8.19 (*m*, 2 arom. H); 8.49 (*s*, H–C(8)); 8.60 (*s*, H–C(2)); 10.14 (br. *s*, exchanged with D_2O, NH). ^{13}C-NMR (75 MHz, (D_6)acetone): 166.2 (*s*, C=O); 152.4 (*d*, C(2)); 152.2 (*s*, C(6)); 151.4 (*s*, C(4)); 144.3 (*d*, C(8)); 134.8 (*s*); 133.3 (*d*); 129.5 (2*d*); 129.4 (2*d*); 125.9 (*s*, C(5)); 104.7 (*s*, C(6′)); 90.80 (*s*, C(7′)); 90.74 (*d*, C(1′)); 90.2 (*d*, C(4′)); 74.9 (*d*, C(2′)); 72.0 (*d*, C(3′)); 64.2 (*d*, C(5′)); 0.0 (*q*, Me_3Si). FAB-MS: 468 ($[M+1]^+$). Anal. calc. for $C_{22}H_{25}N_5O_5Si$ (467.56): C 56.52, H 5.39, N 14.98; found: C 56.46, H 5.63, N 14.91.

*9-(6,7-Dideoxy-β-*D*-allo-hept-6-ynofuranosyl)adenine* (**7**). At 25°, a soln. of **6** (22.3 mg, 48.1 μmol) in MeOH (0.56 ml) was treated with 25% aq. NH_4OH (0.56 ml), stirred at 60° for 2 h, evaporated, suspended in MeOH (2.0 ml), treated with SiO_2 (77.1 mg), evaporated, and loaded on a silica-gel column. FC (1.3 g of silica gel; $CHCl_3$/MeOH 3:1) gave **7** (12.0 mg, 86%). White solid. R_f($CHCl_3$/MeOH 3:1) 0.48. M.p. 208° (dec.; MeOH). $[\alpha]_D^{25} = -108.1$ ($c = 1.03$, DMSO). UV (DMSO): 266.0 (13000). ^{1}H-NMR (300 MHz, (D_6)DMSO): 3.40 (*d*, $J = 2.2$, H–C(7′)); 3.98 (*dd*, $J = 4.5$, 0.5, H–C(4′)); 4.23 (br. *s*, addn. of D_2O → *dd*, $J = 5.9$, 0.5, H–C(3′)); 4.49 (br. *s*, addn. of D_2O → *dd*, $J = 4.5$, 2.2, H–C(5′)); 4.60–4.72 (*m*, addn. of D_2O → 4.63, *dd*, $J = 8.6$, 5.9, H–C(2′)); 5.35 (br. *d*, $J = 4.5$, exchanged with D_2O, OH); 5.46 (br. *d*, $J = 6.3$, exchanged with D_2O, OH); 5.91 (*d*, $J = 8.6$, H–C(1′)); 6.57 (br. *d*, $J = 3.8$, exchanged with D_2O, OH); 7.40 (br. *s*, exchanged with D_2O, NH_2); 8.14 (*s*, H–C(8)); 8.30 (*s*, H–C(2)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.1 (*s*, C(6)); 152.2 (*d*, C(2)); 148.9 (*s*, C(4)); 139.8 (*d*, C(8)); 119.3 (*s*, C(5)); 88.2 (*d*, C(1′)); 87.6 (*d*, C(4′)); 82.7 (*d*, C(7′)); 76.0 (*s*, C(6′)); 73.1 (*d*, C(2′)); 70.3 (*d*, C(3′)); 61.7 (*d*, C(5′)). FAB-MS: 292 ($[M+1]^+$). Anal. calc. for $C_{12}H_{13}N_5O_4$ (291.27): C 49.48, H 4.50, N 24.04; found: C 49.68, H 4.77, N 23.84.

N^6*-Benzoyl-9-[6,7-dideoxy-7-*C*-(trimethylsilyl)-α-*L*-talo-hept-6-ynofuranosyl]adenine* (**8**). At 25°, a soln. of **3** (88.1 mg, 0.174 mmol) in 80% aq. HCOOH (4.4 ml) was stirred for 10 h, evaporated, and co-evaporated several times with PhMe. FC (5.0 g of silica gel; $CHCl_3$/MeOH 6:1) gave **8** (55.2 mg, 64%). White solid. R_f ($CHCl_3$/MeOH 7:1) 0.48. M.p. 143°. $[\alpha]_D^{25} = +2.2$ ($c = 1.01$, MeOH). UV (MeOH): 277.0 (16000); 231.0 (12000). IR (KBr): 3331*m*, 2957*w*, 2173*w*, 1703*m*, 1614*s*, 1584*s*, 1515*m*, 1458*s*, 1411*m*, 1331*m*, 1299*m*, 1250*s*, 1090*m*, 1071*m*, 966*w*, 894*w*, 845*s*, 797*m*, 760*m*. ^{1}H-NMR (300 MHz, (D_6)acetone + D_2O): 0.11 (*s*, Me_3Si); 4.20 (*dd*, $J =$ 3.8, 2.5, H–C(4′)); 4.41 (*dd*, $J = 5.8$, 2.5, H–C(3′)); 4.67 (*d*, $J = 3.8$, H–C(5′)); 4.83 (*dd*, $J = 7.2$, 5.8, H–C(2′)); 6.16 (*d*, $J = 7.2$, H–C(1′)); 7.49–7.69 (*m*, 3 arom. H); 8.09–8.19 (*m*, 2 arom. H); 8.51 (*s*, H–C(8)); 8.62 (*s*, H–C(2)). ^{13}C-NMR (75 MHz, (D_6)acetone): 152.5 (*d*, C(2)); 152.2 (*s*, C(6)); 151.3 (*s*, C(4)); 144.0 (*d*, C(8)); 134.9 (*s*); 133.3 (*d*); 129.4 (2*d*); 129.3 (2*d*); 125.8 (*s*, C(5)); 106.3 (*s*, C(6′)); 90.3 (*d*, C(1′)); 89.4 (*s*, C(7′)); 89.3 (*d*, C(4′)); 74.8 (*d*, C(2′)); 72.7 (*d*, C(3′)); 63.7 (*d*, C(5′)); 0.0 (*q*, Me_3Si). FAB-MS: 468 ($[M+1]^+$).

*9-(6,7-Dideoxy-α-*L*-talo-hept-6-ynofuranosyl)adenine* (**9**). At 25°, a soln. of **8** (52.2 mg, 0.112 mmol) in MeOH (1.3 ml) was treated with 25% aq. NH_4OH (1.3 ml), stirred at 60° for 2 h, evaporated, suspended in MeOH (6.0 ml), treated with SiO_2 (223.6 mg), evaporated, and charged on a silica gel column. FC (3.0 g of silica gel; $CHCl_3$/MeOH 3:1) gave **9** (31.3 mg, 96%). White solid. R_f($CHCl_3$/EtOH 7:4) 0.46. M.p. 166° (dec.; DMSO/CH_2Cl_2). $[\alpha]_D^{25} = +0.1$ ($c = 1.00$, MeOH). UV (MeOH): 257.0 (9800), 218.0 (7000). ^{1}H-NMR (300 MHz, CD_3OD): 2.83 (*d*, $J = 2.9$, H–C(7′)); 4.19 (*dd*, $J = 4.3$, 2.0, H–C(4′)); 4.32 (*dd*, $J = 6.1$, 2.0, H–C(3′)); 4.61 (*dd*, $J = 4.3$, 2.9, H–C(5′)); 4.79 (*dd*, $J = 7.9$, 6.1, H–C(2′)); 6.01 (*d*, $J = 7.9$, H–C(1′)); 8.19 (*s*, H–C(8)); 8.31 (*s*, H–C(2)). ^{13}C-NMR (75 MHz, CD_3OD): 157.6 (*s*, C(6)); 153.6 (*d*, C(2)); 150.1 (*s*, C(4)); 142.0 (*d*, C(8)); 121.0 (*s*, C(5)); 90.9 (*d*, C(1′)); 89.9 (*d*, C(4′)); 83.5 (*d*, C(7′)); 75.2 (*d*, C(2′)); 74.7 (*s*, C(6′)); 72.9 (*d*, C(3′)); 63.6 (*d*, C(5′)). FAB-MS: 292 ($[M+1]^+$).

N^6*-Benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-7-*C*-(trimethylsilyl)-β-*D*-allo-hept-6-ynofuranosyl]adenine* (**10**). At 25°, a soln. of **2** (101.9 mg, 0.201 mmol) and imidazole (44.7 mg, 0.657 mmol) in dry DMF (3.1 ml) was treated dropwise with Et_3SiCl (100 μl, 0.596 mmol), stirred for 6 h, and poured into ice-water (*ca.* 10 ml). After extraction with hexane/AcOEt 1:1 (3 × 2.0 ml), the combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (3.5 g of silica gel; hexane/AcOEt 1:1) gave **10** (104.8 mg, 84%). Yellow solid. R_f (hexane/AcOEt 1:2) 0.42. M.p. 72°. $[\alpha]_D^{25} = -82.8$ ($c = 1.04$, $CHCl_3$). UV ($CHCl_3$): 279.0 (20000). IR ($CHCl_3$): 3408*w*, 3008*s*, 2961*s*, 2913*m*, 2887*m*, 2173*w*, 1708*s*, 1612*s*, 1584*s*, 1519*s*, 1478*s*, 1455*s*, 1421*s*, 1385*m*, 1353*m*, 1330*m*, 1295*m*, 1248*s*, 1157*m*, 1089*s*, 1048*s*, 1030*m*, 967*m*, 928*s*, 848*s*, 818*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.14 (*s*, Me_3Si); 0.56–0.73 (*m*, ($MeCH_2)_3Si$); 0.92 (*t*, $J = 8.6$, ($MeCH_2)_3Si$); 1.43, 1.65 (2*s*, Me_2C); 7.47–7.63 (*m*, 3 arom. H); 7.97–8.06 (*m*, 2 arom. H); 9.10 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.6 (*s*, C=O); 153.0 (*d*, C(2)); 151.3 (*s*, C(6)); 149.5 (*s*, C(4)); 141.5 (*d*, C(8)); 133.8 (*s*); 132.7 (*d*); 128.9 (2*d*); 127.9 (2*d*); 123.2 (*s*, C(5)); 114.2 (*s*, Me_2C); 102.6 (*s*, C(6′)); 92.7 (*s*, C(7′)); 92.0 (*d*, C(1′)); 89.2 (*d*, C(4′)); 84.7 (*d*, C(2′)); 81.4 (*d*, C(3′)); 63.9 (*d*, C(5′)); 27.3, 25.4 (2*q*, Me_2C); 6.7 (*q*, ($MeCH_2)_3Si$); 4.8 (*t*, ($MeCH_2)_3Si$); −0.5 (*q*, Me_3Si). FAB-MS: 622 ($[M+1]^+$). Anal. calc. for $C_{31}H_{43}N_5O_5Si_2$ (621.88): C 59.87, H 6.97, N 11.26; found: C 59.76, H 7.20, N 11.14.

N^6*-Benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-7-*C*-(trimethylsilyl)-α-*L*-talo-hept-6-ynofuranosyl]adenine* (**11**). At 25°, a soln. of **3** (61.8 mg, 0.122 mmol) and imidazole (26.5 mg, 0.389 mmol) in dry DMF (1.9 ml) was treated dropwise with Et_3SiCl (61 μl, 0.363 mmol), stirred for 5 h, poured into ice-water (*ca.* 5 ml), and extracted with hexane/AcOEt 1:1 (3 × 3.0 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (3.0 g of silica gel; hexane/AcOEt 4:5) gave **11** (43.7 mg, 58%). Yellow solid. R_f(hexane/AcOEt 1:2) 0.52. M.p. 66–67°. $[\alpha]_D^{25} = +7.6$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 279.0 (19000). IR ($CHCl_3$): 3408*w*, 3008*m*, 2960*m*, 2913*w*, 2888*w*, 2175*w*, 1708*s*, 1612*s*, 1584*s*, 1517*w*, 1455*s*, 1405*w*,

1385*m*, 1351*m*, 1328*m*, 1293*m*, 1252*s*, 1157*m*, 1130*m*, 1093*s*, 1004*m*, 978*w*, 930*w*, 846*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.17 (*s*, Me_3Si); 0.48–0.64 (*m*, $(MeCH_2)_3Si$); 0.86 (*t*, $J = 9.0$, $(MeCH_2)_3Si$); 1.42, 1.65 (2*s*, Me_2C); 7.47–7.64 (*m*, 3 arom. H); 7.97–8.06 (*m*, 2 arom. H); 9.12 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.6 (*s*, C=O); 153.0 (*d*, C(2)); 151.1 (*s*, C(6)); 149.2 (*s*, C(4)); 141.8 (*d*, C(8)); 133.9 (*s*); 132.7 (*d*); 128.9 (2*d*); 127.8 (2*d*); 123.1 (*s*, C(5)); 114.2 (*s*, Me_2C); 103.3 (*s*, C(6′)); 92.9 (*d*, C(1′)); 92.0 (*s*, C(7′)); 89.3 (*d*, C(4′)); 85.3 (*d*, C(2′)); 82.0 (*d*, C(3′)); 64.0 (*d*, C(5′)); 27.2, 25.4 (2*q*, Me_2C); 6.6 (*q*, $(MeCH_2)_3Si$); 4.5 (*t*, $(MeCH_2)_3Si$); −0.4 (*q*, Me_3Si). FAB-MS: 622 ($[M+1]^+$). Anal. calc. for $C_{31}H_{43}N_5O_5Si_2 \cdot 0.5\,H_2O$ (630.89): C 59.12, H 7.03, N 11.10; found: C 58.98, H 6.91, N 11.00.

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**12**). At 25°, a soln. of **1** (9.10 g, 22.1 mmol) and imidazole (3.89 g, 57.1 mmol) in dry DMF (270 ml) was treated dropwise with Et_3SiCl (5.6 ml, 33.4 mmol), stirred for 10 h, poured into ice-water (*ca.* 600 ml), and extracted with Et_2O/AcOEt 1:1 (4 × 400 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (400 g of silica gel; $CHCl_3$/AcOEt 5:3) gave **12** (11.27 g, 97%). White solid. R_f($CHCl_3$/AcOEt 2:1) 0.41. M.p. 56–58°. $[\alpha]_D^{25} = -52.1$ ($c = 1.07$, $CHCl_3$). UV ($CHCl_3$): 276.0 (15000). IR ($CHCl_3$): 3407*w*, 3008*s*, 2959*s*, 2913*m*, 2878*w*, 1708*s*, 1612*s*, 1585*s*, 1504*m*, 1479*s*, 1456*s*, 1403*m*, 1385*m*, 1353*m*, 1326*m*, 1292*m*, 1248*s*, 1156*m*, 1134*s*, 1090*s*, 1003*m*, 969*w*, 928*w*, 858*w*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.54 (*q*, $J = 8.8$, $(MeCH_2)_3Si$); 0.88 (*t*, $J = 8.8$, $(MeCH_2)_3Si$); 1.40, 1.64 (2*s*, Me_2C); 7.47–7.63 (*m*, 3 arom. H); 7.98–8.05 (*m*, 2 arom. H); 9.09 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.9 (*s*, C=O); 153.1 (*d*, C(2)); 151.5 (*s*, C(6)); 149.8 (*s*, C(4)); 141.9 (*d*, C(8)); 134.1 (*s*); 133.0 (*d*); 129.1 (2*d*); 128.1 (2*d*); 123.5 (*s*, C(5)); 114.4 (*s*, Me_2C); 92.0 (*d*, C(1′)); 87.7 (*d*, C(4′)); 85.3 (*d*, C(2′)); 81.7 (*d*, C(3′)); 63.3 (*t*, C(5′)); 27.3, 25.4 (2*q*, Me_2C); 6.7 (*q*, $(MeCH_2)_3Si$); 4.1 (*t*, $(MeCH_2)_3Si$). FAB-MS: 526 ($[M+1]^+$). Anal. calc. for $C_{26}H_{35}N_5O_5Si$ (525.68): C 59.41, H 6.71, N 13.32; found: C 59.41, H 6.73, N 13.14.

N^6-*Benzoyl-8-chloro-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**13**). A soln. of $(i\text{-}Pr)_2NH$ (1.0 ml, 7.14 mmol) in dry THF (23 ml) was cooled to 0°, treated dropwise with 1.6M BuLi in hexane (4.6 ml, 7.14 mmol), stirred for 30 min, cooled to −78°, treated dropwise with a soln. of **12** (1.551 g, 2.95 mmol) in dry THF (23 ml), stirred for 3 h, treated with $PhSO_2Cl$ (1.1 ml, 8.63 mmol), stirred for 1 h, and without cooling, treated with sat. aq. NH_4Cl soln. (20 ml) and H_2O (20 ml). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 30 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (70 g of silica gel; hexane/AcOEt 5:4) gave **13** (1.603 g, 97%). Light yellow solid. R_f(hexane/AcOEt 3:2) 0.30. M.p. 56°. $[\alpha]_D^{25} = -15.7$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 280.0 (19000). IR ($CHCl_3$): 3406*w*, 3008*s*, 2976*s*, 2913*m*, 2878*m*, 1711*m*, 1611*s*, 1589*s*, 1514*m*, 1478*s*, 1450*s*, 1420*m*, 1385*m*, 1322*m*, 1248*s*, 1161*m*, 1087*s*, 1046*s*, 972*w*, 928*s*, 875*m*, 850*m*, 818*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.49 (*q*, $J = 8.0$, $(MeCH_2)_3Si$); 0.87 (*t*, $J = 8.0$, $(MeCH_2)_3Si$); 1.41, 1.62 (2*s*, Me_2C); 7.47–7.65 (*m*, 3 arom. H); 7.95–8.05 (*m*, 2 arom. H); 8.92 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.7 (*d*, C(2)); 151.8 (*s*, C(6)); 148.5 (*s*, C(4)); 141.8 (*s*,

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for Adenosines* **1** *and* **12**–**16**

	1	**12**	**13**	**14**	**15**	**16**
H–C(2)	8.79	8.83	8.77	8.77	8.73	8.71
H–C(8)	8.07	8.27	–	–	–	–
H–C(1′)	5.94	6.25	6.25	6.17	6.14	6.08
H–C(2′)	5.24	5.26	5.76	5.32	5.81	5.32
H–C(3′)	5.12	4.95	5.16	5.11	5.18	5.10
H–C(4′)	4.56	4.45	4.31	4.55	4.32	4.55
H_a–C(5′)	3.80	3.75	3.66	3.82	3.65	3.81
H_b–C(5′)	3.99	3.87	3.76	4.00	3.76	3.98
HO–C(5′)	5.75	–	–	5.57	–	5.75
J(1′,2′)	4.8	2.7	2.3	5.0	2.3	5.5
J(2′,3′)	6.0	6.0	6.5	5.8	6.3	5.5
J(3′,4′)	< 1.0	2.5	3.7	1.5	3.5	0.8
J(4′,5a′)	1.8	4.0	6.0	2.0	6.5	2.0
J(4′,5b′)	1.5	3.7	6.0	2.0	6.5	1.5
J(5a′,5b′)	13.0	11.0	10.5	13.1	10.5	13.0
J(5a′,OH)	11.0	–	–	11.0	–	11.5
J(5b′,OH)	1.5	–	–	2.0	–	1.5

C(8)); 133.5 (*s*); 133.0 (*d*); 128.9 (2*d*); 127.8 (2*d*); 121.8 (*s*, C(5)); 114.4 (*s*, Me_2C); 90.6 (*d*, C(1′)); 88.2 (*d*, C(4′)); 82.9 (*d*, C(2′)); 81.9 (*d*, C(3′)); 62.7 (*t*, C(5′)); 27.2, 25.5 (2*q*, *Me*$_2$C); 6.6 (*q*, (*Me*CH_2)$_3$Si); 4.2 (*t*, (MeCH_2)$_3$Si). FAB-MS: 560 (100, $[M+1]^+$), 562 (44). Anal. calc. for $C_{26}H_{34}ClN_5O_5Si$ (560.12): C 55.75, H 6.12, N 12.50; found: C 55.72, H 6.07, N 12.31.

N^6-*Benzoyl-8-chloro-2′,3′*-O-*isopropylideneadenosine* (**14**). A soln. of **13** (4.10 g, 7.30 mmol) in dry THF (123 ml) was treated with a 1.0M soln. of TBAF in THF (11.0 ml, 11.0 mmol), stirred for 15 h, and evaporated. FC (200 g of silica gel; $CHCl_3$/acetone 3:1) gave **14** (3.772 g, 100%). Light yellow solid. R_f($CHCl_3$/acetone 3:1) 0.48. M.p. 173°. $[\alpha]_D^{25} = -88.5$ ($c = 1.06$, $CHCl_3$). UV ($CHCl_3$): 275.0 (15000). IR ($CHCl_3$): 3401*w*, 3007*m*, 2948*w*, 2874*w*, 1713*s*, 1610*s*, 1592*s*, 1481*s*, 1450*s*, 1423*m*, 1385*m*, 1375*m*, 1356*m*, 1322*s*, 1300*m*, 1248*s*, 1168*w*, 1155*w*, 1112*s*, 1085*s*, 1030*w*, 1000*w*, 968*w*, 952*w*, 928*w*, 894*w*, 851*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 2*; additionally, 1.40, 1.68 (2*s*, Me_2C); 7.50–7.67 (*m*, 3 arom. H); 7.96–8.05 (*m*, 2 arom. H); 9.00 (br *s*, exchanged with D_2O, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 152.4 (*d*, C(2)); 151.3 (*s*, C(6)); 149.1 (*s*, C(8), C(4)); 133.3 (*s*); 133.1 (*d*); 129.0 (2*d*); 127.9 (2*d*); 122.3 (*s*, C(5)); 114.3 (*s*, Me_2C); 92.8 (*d*, C(1′)); 85.9 (*d*, C(4′)); 82.5 (*d*, C(2′)); 81.5 (*d*, C(3′)); 63.2 (*t*, C(5′)); 27.7, 25.4 (2*q*, *Me*$_2$C). FAB-MS: 274 (100), 276 (39), 446 (24, $[M+1]^+$), 448 (9). Anal. calc. for $C_{20}H_{20}ClN_5O_5$ (445.86): C 53.88, H 4.52, N 15.71; found: C 53.92, H 4.72, N 15.76.

N^6-*Benzoyl-8-iodo-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**15**). A soln. of (i-Pr)$_2$NH (1.0 ml, 7.14 mmol) in dry THF (23 ml) was cooled to 0°, treated dropwise with 1.6M BuLi in hexane (4.6 ml, 7.14 mmol), stirred for 30 min, cooled to −78°, treated dropwise with a soln. of **12** (1.564 g, 2.98 mmol) in dry THF (23 ml), stirred for 3 h, treated with I_2 (1.19 g, 4.69 mmol), stirred for 1 h, and without cooling, treated with sat. aq. NH_4Cl soln. (30 ml) and sat. aq. $Na_2S_2O_3$ soln. (15 ml). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 20 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (85 g of silica gel; hexane/AcOEt 5:4) gave **15** (1.76 g, 91%). Yellow solid. R_f(hexane/AcOEt 5:4) 0.39. M.p. 78–80°. $[\alpha]_D^{25} = -16.1$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 290.0 (22000), 245.0 (15000). IR ($CHCl_3$): 3405*w*, 3007*m*, 2957*m*, 2913*w*, 2877*m*, 1710*s*, 1608*s*, 1588*s*, 1504*m*, 1486*m*, 1461*s*, 1422*s*, 1384*m*, 1376*m*, 1355*m*, 1315*m*, 1270*s*, 1284*m*, 1160*m*, 1088*s*, 1005*m*, 972*w*, 872*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.49 (*q*, J = 8.3, (MeCH_2)$_3$Si); 0.87 (*t*, J = 8.3, (*Me*CH_2)$_3$Si); 1.41, 1.63 (2*s*, Me_2C); 7.47–7.65 (*m*, 3 arom. H); 7.95–8.04 (*m*, 2 arom. H); 8.98 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.4 (*d*, C(2)); 151.8 (*s*, C(6)); 148.3 (*s*, C(4)); 133.6 (*s*); 133.0 (*d*); 128.9 (2*d*); 127.8 (2*d*); 125.5 (*s*, C(5)); 114.2 (*s*, Me_2C); 104.8 (*s*, C(8)); 93.8 (*d*, C(1′)); 88.3 (*d*, C(4′)); 82.9 (*d*, C(2′)); 82.1 (*d*, C(3′)); 62.8 (*t*, C(5′)); 27.3, 25.5 (2*q*, *Me*$_2$C); 6.6 (*q*, (*Me*CH_2)$_3$Si); 4.2 (*t*, (MeCH_2)$_3$Si). FAB-MS: 652 ($[M+1]^+$). Anal. calc. for $C_{26}H_{34}IN_5O_5Si$ (651.58): C 47.93, H 5.26, N 10.75; found: C 47.93, H 5.24, N 10.61.

N^6-*Benzoyl-8-iodo-2′,3′*-O-*isopropylideneadenosine* (**16**). At 25°, a soln. of **15** (3.17 g, 4.87 mmol) in dry THF (95 ml) was treated with 1.0M soln. of TBAF · 3 H_2O in THF (7.3 ml, 7.31 mmol), and stirred. After 10 h, the mixture was concentrated. FC (150 g of silica gel; $CHCl_3$/acetone 3:1) gave **16** (2.45 g, 94%). White solid. R_f($CHCl_3$/acetone 3:1) 0.52. M.p. 210° (dec.). $[\alpha]_D^{25} = -75.9$ ($c = 0.82$, $CHCl_3$). UV ($CHCl_3$): 291.0 (22000); 245.0 (15000). IR ($CHCl_3$): 3401*w*, 3008*m*, 2938*m*, 2872*w*, 1713*s*, 1607*s*, 1504*w*, 1480*m*, 1462*m*, 1449*m*, 1423*s*, 1385*m*, 1375*m*, 1356*m*, 1316*m*, 1269*m*, 1252*m*, 1166*w*, 1112*m*, 1086*s*, 1030*w*, 995*w*, 968*w*, 951*w*, 891*w*, 851*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 1.40, 1.72 (2*s*, Me_2C); 7.48–7.66 (*m*, 3 arom. H); 7.95–8.04 (*m*, 2 arom. H); 9.01 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 152.1 (*d*, C(2)); 151.3 (*s*, C(6)); 148.9 (*s*, C(4)); 133.4 (*s*); 133.0 (*d*); 129.0 (2*d*); 127.9 (2*d*); 126.2 (*s*, C(5)); 114.3 (*s*, Me_2C); 103.8 (*s*, C(8)); 95.8 (*d*, C(1′)); 85.7 (*d*, C(4′)); 82.3 (*d*, C(2′)); 81.6 (*d*, C(3′)); 63.3 (*t*, C(5′)); 27.8, 25.5 (2*q*, *Me*$_2$C). FAB-MS: 537.8 ($[M+1]^+$). Anal. calc. for $C_{20}H_{20}IN_5O_5$ (537.31): C 44.71, H 3.75, N 13.03; found: C 44.97, H 4.01, N 12.99.

N^6-*Benzoyl-8-chloro-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-adenine* (**17**) *and* N^6-*Benzoyl-8-chloro-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]adenine* (**18**). At 15°, a soln. of **14** (3.772 g, 8.45 mmol) and DCC (5.10 g, 24.7 mmol) in dry DMSO (21 ml) was treated dropwise with $Cl_2CHCOOH$ (0.35 ml, 4.24 mmol), stirred for 10 min, warmed to 25°, stirred for 90 min, and filtered. The residue was washed with small amounts of DMSO, and the combined filtrates were washed with hexane (4 × 100 ml). The DMSO layer was diluted with $CHCl_3$ (550 ml), washed with H_2O (2 × 200 ml), dried (Na_2SO_4), and evaporated affording the crude aldehyde. At 0°, a soln. of EtMgBr (25.0 mmol) in THF (38 ml) was treated dropwise with (trimethylsilyl)acetylene (3.6 ml, 25.4 mmol), stirred for 10 min, warmed to 25°, stirred for 30 min, cooled to 0°, and treated with a soln. of the crude aldehyde in dry THF (113 ml). After 3 h, the mixture was treated with sat. aq. NH_4Cl soln. (75 ml) and H_2O (25 ml). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 50 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (400 g of silica gel; C_6H_6/Et_2O/AcOEt 5:1:2) gave **18** (794 mg, 17%), **17**/**18** (428.5 mg, 9%), and **17** (726 mg, 16%).

Data of **17**: Yellow solid. R_f($CHCl_3$/AcOEt 7:2) 0.53. M.p. 108°. $[\alpha]_D^{25} = -137.9$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 280.0 (18000). IR ($CHCl_3$): 3403*w*, 3203*w*, 3008*m*, 2963*w*, 2181*w*, 1714*m*, 1610*s*, 1594*s*, 1481*s*, 1450*s*, 1423*w*, 1385*m*, 1358*m*, 1343*w*, 1324*s*, 1302*m*, 1252*s*, 1168*w*, 1155*w*, 1112*s*, 1089*s*, 1046*w*, 1028*w*, 1001*w*, 972*w*, 894*w*, 849*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.21 (*s*, Me_3Si); 1.41, 1.68 (2*s*, Me_2C); 7.46–7.65 (*m*, 3 arom. H); 7.94–8.04 (*m*, 2 arom. H); 8.99 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 152.2 (*d*, C(2)); 150.9 (*s*, C(6)); 149.3 (*s*, C(4)); 141.1 (*s*, C(8)); 133.2 (*s*); 133.1 (*d*); 129.0 (2*d*); 127.9 (2*d*); 122.3 (*s*, C(5)); 114.3 (*s*, Me_2C); 101.1 (*s*, C(6′)); 93.2 (*d*, C(1′)); 92.2 (*s*, C(7′)); 87.3 (*d*, C(4′)); 81.9 (*d*, C(2′)); 80.6 (*d*, C(3′)); 63.5 (*d*, C(5′)); 27.7, 25.4 (2*q*, Me_2C); −0.2 (*q*, Me_3Si). FAB-MS: 274 (100), 276 (33), 542 (22, $[M+1]^+$), 544 (8).

Data of **18**: Yellow solid. R_f($CHCl_3$/AcOEt 3:2) 0.55. M.p. 173° ($CHCl_3$/hexane). $[\alpha]_D^{25} = +0.1$ ($c = 1.05$, $CHCl_3$). UV ($CHCl_3$): 280.0 (17000). IR ($CHCl_3$): 3402*w*, 3252*w*, 3008*m*, 2962*w*, 2175*w*, 1713*m*, 1610*s*, 1593*s*, 1481*s*, 1450*s*, 1422*m*, 1385*m*, 1358*m*, 1324*s*, 1251*s*, 1168*w*, 1155*m*, 1118*s*, 1088*s*, 1030*w*, 973*w*, 928*w*, 848*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.11 (*s*, Me_3Si); 1.38, 1.66 (2*s*, Me_2C); 7.50–7.67 (*m*, 3 arom. H); 7.97–8.04 (*m*, 2 arom. H); 8.88 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.3 (*d*, C(2)); 151.3 (*s*, C(6)); 149.1 (*s*, C(4)); 141.1 (*s*, C(8)); 133.2 (*s*); 133.1 (*d*); 129.0 (2*d*); 127.9 (2*d*); 122.3 (*s*, C(5)); 114.6 (*s*, Me_2C); 102.8 (*s*, C(6′)); 92.8 (*d*, C(1′)); 90.4 (*s*, C(7′)); 87.2 (*d*, C(4′)); 82.3 (*d*, C(2′)); 81.7 (*d*, C(3′)); 63.6 (*d*, C(5′)); 27.6, 25.4 (2*q*, Me_2C); −0.2 (*q*, Me_3Si). FAB-MS: 274 (100), 276 (35), 542 (52, $[M+1]^+$), 544 (23).

5′,8-Anhydro-N^6*-benzoyl-9-[6,7-dideoxy-2,3*-O*-isopropylidene-7*-C*-(trimethylsilyl)-β*-D-allo*-hept-6-ynofuranosyl]-8-hydroxyadenine* (**19**). At 25°, a soln. of **17** (41.6 mg, 76.7 μmol) in PhMe (1.2 ml) was treated with DBU (17 μl, 0.113 mmol), stirred at 50° for 90 min, diluted with AcOEt (3 ml), washed with sat. aq. $NaHCO_3$ soln. (0.5 ml) and brine (0.5 ml), dried (Na_2SO_4), and evaporated. FC (12 g of silica gel; $CHCl_3$/AcOEt 9:4) gave **19** (29.3 mg, 76%). Yellow solid. R_f ($CHCl_3$/AcOEt 5:2) 0.50. M.p. 142–143°. $[\alpha]_D^{25} = -57.0$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 283.0 (17000), 263.0 (12000). IR ($CHCl_3$): 3408*w*, 3007*m*, 1708*m*, 1616*s*, 1590*m*, 1546*m*, 1500*m*, 1482*m*, 1462*m*, 1429*m*, 1402*m*, 1386*w*, 1378*w*, 1356*m*, 1318*s*, 1253*s*, 1164*m*, 1120*w*, 1094*w*, 1058*s*, 1027*w*, 974*w*, 956*w*, 923*w*, 854*s*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.23 (*s*, Me_3Si); 1.39, 1.57 (2*s*, Me_2C); 4.76 (*d*, $J = 0.8$, irrad. at 4.95 → NOE of 14%, H–C(4′)); 4.80 (*d*, $J = 5.5$, H–C(2′)); 4.95 (*d*, $J = 0.8$, H–C(5′)); 5.26 (*d*, $J = 5.5$, H–C(3′)); 6.45 (*s*, H–C(1′)); 7.43–7.61 (*m*, 3 arom. H); 7.93–8.02 (*m*, 2 arom. H); 8.67 (*s*, H–C(2)); 8.95 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.5 (*s*, C=O); 153.8 (*s*, C(6)); 152.2 (*d*, C(2)); 150.5 (*s*, C(4)); 148.1 (*s*, C(8)); 133.5 (*s*); 132.7 (*d*); 128.8 (2*d*); 127.9 (2*d*); 119.3 (*s*, C(5)); 113.5 (*s*, Me_2C); 97.8 (*s*, C(6′)); 95.2 (*s*, C(7′)); 89.2 (*d*, C(1′)); 87.0 (*d*, C(4′)); 85.5 (*d*, C(2′)); 80.6 (*d*, C(3′)); 76.2 (*d*, C(5′)); 26.1, 24.7 (2*q*, Me_2C); −0.5 (*q*, Me_3Si). FAB-MS: 506 ($[M+1]^+$).

5′,8-Anhydro-N^6*-benzoyl-9-[6,7-dideoxy-2,3*-O*-isopropylidene-7*-C*-(trimethylsilyl)-α*-L-talo*-hept-6-ynofuranosyl]-8-hydroxyadenine* (**20**). At 25°, a soln. of **18** (147.9 mg, 0.273 mmol) in PhMe (4.4 ml) was treated with DBU (61 μl, 0.410 mmol), stirred at 50° for 90 min, diluted with AcOEt (12 ml), washed with sat. aq. $NaHCO_3$ soln. (5.0 ml) and brine (3.0 ml), dried (Na_2SO_4), and evaporated. FC (17 g of silica gel; $CHCl_3$/AcOEt 1:1) gave **20** (92.6 mg, 67%). Yellow solid. R_f($CHCl_3$/AcOEt 1:1) 0.52. M.p. 117°. $[\alpha]_D^{25} = +210.0$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 283.0 (17000), 248.0 (12000). IR ($CHCl_3$): 3407*w*, 3006*m*, 1708*s*, 1618*s*, 1590*s*, 1549*m*, 1500*m*, 1483*s*, 1463*s*, 1431*s*, 1402*s*, 1386*m*, 1377*m*, 1358*m*, 1321*m*, 1296*w*, 1252*s*, 1163*m*, 1119*w*, 1103*w*, 1056*s*, 1027*w*, 1004*w*, 977*w*, 957*w*, 853*s*, 832*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): −0.03 (*s*, Me_3Si); 1.36, 1.56 (2*s*, Me_2C); 4.73 (*d*, $J = 2.3$, irrad. at 5.20 → NOE of 15%, H–C(4′)); 4.81 (*d*, $J = 5.5$, H–C(2′)); 5.08 (*d*, $J = 5.5$, irrad. at 5.20 → NOE of 7.8%, H–C(3′)); 5.20 (*d*, $J = 2.3$, H–C(5′)); 6.49 (*s*, H–C(1′)); 7.45–7.63 (*m*, 3 arom. H); 7.93–8.02 (*m*, 2 arom. H); 8.77 (*s*, H–C(2)); 8.86 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 153.6 (*s*, C(6)); 152.4 (*d*, C(2)); 150.2 (*s*, C(4)); 147.9 (*s*, C(8)); 133.7 (*s*); 132.7 (*d*); 128.9 (2*d*); 127.7 (2*d*); 119.3 (*s*, C(5)); 113.7 (*s*, Me_2C); 99.2 (*s*, C(6′)); 94.6 (*s*, C(7′)); 87.9 (*d*, C(1′)); 86.8 (*d*, C(4′)); 85.3 (*d*, C(2′)); 81.5 (*d*, C(3′)); 74.3 (*d*, C(5′)); 26.1, 24.7 (2*q*, Me_2C); −0.7 (*q*, Me_3Si). FAB-MS: 506 ($[M+1]^+$). Anal. calc. for $C_{25}H_{27}N_5O_5Si \cdot H_2O$ (523.62): C 57.35, H 5.58, N 13.37; found: C 57.56, H 5.44, N 13.37.

N^6*-Benzoyl-8-chloro-9-[6,7-dideoxy-2,3*-O*-isopropylidene-5*-O*-(triethylsilyl)-7*-C*-(trimethylsilyl)-β*-D-allo*-hept-6-ynofuranosyl]adenine* (**21**). At 25°, a soln. of **17** (56.2 mg, 0.104 mmol) and imidazole (30.0 mg, 0.441 mmol) in dry DMF (1.7 ml) was treated dropwise with Et_3SiCl (52 μl, 0.31 mmol), stirred for 12 h, poured into ice-water (*ca.* 10 ml), and extracted with hexane/AcOEt 1:1 (3 × 3.0 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (2.0 g of silica gel; hexane/AcOEt 3:2) gave **21** (48.9 mg, 72%). Light orange solid. R_f (hexane/AcOEt 3:2) 0.48. M.p. 74°. $[\alpha]_D^{25} = +5.4$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 280.0 (21000). IR ($CHCl_3$): 3406*w*, 3007*m*, 2959*m*, 2913*w*, 2877*w*, 2174*w*, 1711*m*, 1612*s*, 1589*s*, 1508*w*, 1480*m*, 1450*s*, 1415*w*, 1384*m*, 1376*m*, 1356*w*, 1323*m*, 1248*s*, 1160*m*, 1089*s*, 1004*m*, 892*w*, 847*s*, 818*w*, 595*w*, 568*w*, 514*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.09 (*s*, Me_3Si); 0.52–0.75 (*m*, $(MeCH_2)_3Si$); 0.95 (*t*, $J = 8.5$, $(MeCH_2)_3Si$); 1.41, 1.61 (2*s*, Me_2C); 7.49–7.66 (*m*, 3 arom. H); 7.96–8.05 (*m*, 2 arom. H); 8.90 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 152.7 (*d*, C(2)); 151.7 (*s*, C(6)); 148.5 (*s*, C(4)); 142.1 (*s*,

C(8)); 133.5 (*s*); 133.0 (*d*); 129.0 (2*d*); 127.8 (2*d*); 121.7 (*s*, C(5)); 114.2 (*s*, Me_2C); 103.6 (*s*, C(6′)); 91.0 (*s*, C(7′)); 91.0 (*d*, C(1′)); 89.8 (*d*, C(4′)); 82.4 (2*d*, C(2′), C(3′)); 63.0 (*d*, C(5′)); 27.1, 25.4 (2*q*, Me_2C); 6.7 (*q*, $(MeCH_2)_3Si$); 4.8 (*t*, $(MeCH_2)_3Si$); −0.4 (*q*, Me_3Si). FAB-MS: 656 (100, M^+), 657 (48), 658 (46), 659 (19). Anal. calc. for $C_{31}H_{42}ClN_5O_5Si_2$ (656.33): C 56.73, H 6.45, N 10.67; found: C 56.64, H 6.34, N 10.63.

N^6-*Benzoyl-8-chloro-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]adenine* (**22**). At 25°, a soln. of **18** (213.1 mg, 0.393 mmol) and imidazole (80.7 mg, 1.19 mmol) in dry DMF (6.4 ml) was treated dropwise with Et_3SiCl (0.20 ml, 1.19 mmol), stirred for 16 h, poured into ice-water (*ca.* 15 ml), and extracted with hexane/AcOEt 1:1 (3 × 7.0 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (10 g of silica gel; hexane/AcOEt 3:2) gave **22** (187.8 mg, 73%). Yellow solid. R_f(hexane/AcOEt 3:2) 0.32. M.p. 70°. $[\alpha]_D^{25} = -57.9$ ($c = 1.05$, $CHCl_3$). UV ($CHCl_3$): 283.0 (21000). IR ($CHCl_3$): 3405*w*, 2958*w*, 2877*w*, 2359*m*, 2341*w*, 1711*s*, 1611*s*, 1589*s*, 1480*m*, 1450*s*, 1413*m*, 1384*m*, 1376*m*, 1321*m*, 1252*m*, 1159*m*, 1090*m*, 1040*w*, 1003*m*, 892*m*, 846*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.19 (*s*, Me_3Si); 0.28–0.48 (*m*, $(MeCH_2)_3Si$); 0.76 (*t*, $J = 7.9$, $(MeCH_2)_3Si$); 1.41, 1.62 (2*s*, Me_2C); 7.48–7.66 (*m*, 3 arom. H); 7.95–8.04 (*m*, 2 arom. H); 8.91 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.6 (*s*, C=O); 153.1 (*d*, C(2)); 152.1 (*s*, C(6)); 148.8 (*s*, C(4)); 142.1 (*s*, C(8)); 133.7 (*s*); 133.2 (*d*); 129.2 (2*d*); 128.1 (2*d*); 121.9 (*s*, C(5)); 114.6 (*s*, Me_2C); 103.2 (*s*, C(6′)); 91.8 (*s*, C(7′)); 90.8 (2*d*, C(1′), C(4′)); 82.8 (*d*, C(2′)); 82.2 (*d*, C(3′)); 64.4 (*d*, C(5′)); 27.2, 25.5 (2*q*, Me_2C); 6.4 (*q*, $(MeCH_2)_3Si$); 4.4 (*t*, $(MeCH_2)_3Si$); −0.3 (*q*, Me_3Si). FAB-MS: 656 (100, M^+), 657 (42), 658 (45), 659 (18). Anal. calc. for $C_{31}H_{42}ClN_5O_5Si_2$ (656.33): C 56.73, H 6.45, N 10.67; found: C 56.72, H 6.48, N 10.53.

6-(Benzoylamino)-9-[6,7-dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-7,9-dihydropurine-8-thione* (**23**). At 25°, a soln. of **21** (48.9 mg, 74.5 μmol) in PhMe (2.4 ml) was treated with *N*-phenylthiourea (31.0 mg, 0.204 mmol), stirred at 60° for 25 min, cooled to 25°, diluted with AcOEt (10 ml), washed with sat. aq. $NaHCO_3$ soln. (3 ml) and brine (3 ml), dried (Na_2SO_4), and evaporated. FC (2.0 g of silica gel; hexane/AcOEt 7:4) gave **23** (47.9 mg, 98%). Light yellow solid. R_f(hexane/AcOEt 7:4) 0.46. M.p. 84°. $[\alpha]_D^{25} = -22.4$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 259.0 (24000), 342.0 (22000). IR ($CHCl_3$): 3351*w*, 2993*w*, 2958*m*, 2913*w*, 2877*w*, 2173*w*, 1695*m*, 1623*w*, 1590*m*, 1506*s*, 1490*s*, 1461*s*, 1445*s*, 1412*s*, 1360*m*, 1266*s*, 1251*s*, 1157*m*, 1091*s*, 1002*m*, 873*m*, 846*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.09 (*s*, Me_3Si); 0.60–0.78 (*m*, $(MeCH_2)_3Si$); 0.99 (*t*, $J = 8.5$, $(MeCH_2)_3Si$); 1.37, 1.61 (2*s*, Me_2C); 7.49–7.69 (*m*, 3 arom. H); 7.91–7.99 (*m*, 2 arom. H); 9.17 (br. *s*, BzN*H*); 10.97 (br. *s*, H–N(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.9 (*s*, C=S); 165.8 (*s*, C=O); 152.6 (*s*, C(6)); 151.3 (*d*, C(2)); 138.2 (*s*, C(4)); 133.8 (*d*); 131.5 (*s*); 129.2 (2*d*); 127.7 (2*d*); 114.2 (*s*, Me_2C); 111.2 (*s*, C(5)); 104.8 (*s*, C(6′)); 90.4 (*s*, C(7′)); 89.6, 89.3 (2*d*, C(1′), C(4′)); 82.4, 82.3 (2*d*, C(2′), C(3′)); 63.4 (*d*, C(5′)); 27.3, 25.6 (2*q*, Me_2C); 6.8 (*q*, $(MeCH_2)_3Si$); 4.9 (*t*, $(MeCH_2)_3Si$); −0.2 (*q*, Me_3Si). FAB-MS: 654 ($[M+1]^+$). Anal. calc. for $C_{31}H_{43}N_5O_5SSi_2$ (653.95): C 56.94, H 6.63, N 10.71; found: C 57.07, H 6.53, N 10.66.

6-(Benzoylamino)-9-[6,7-dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]-7,9-dihydropurine-8-thione* (**24**). At 25°, a soln. of **22** (40.3 mg, 61.4 μmol) in PhMe (2.0 ml) was treated with *N*-phenylthiourea (22.6 mg, 0.148 mmol), stirred at 60° for 35 min, diluted with AcOEt (8 ml), washed with sat. aq. $NaHCO_3$ soln. (2.5 ml), and brine (2.5 ml), dried (Na_2SO_4), and evaporated. FC (2.0 g of silica gel; hexane/AcOEt 4:3) gave **24** (33.0 mg, 82%). White solid. R_f(hexane/AcOEt 2:1) 0.48. M.p. 93°. $[\alpha]_D^{25} = -53.5$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 236.0 (22000), 357.0 (26000), 341.0 (23000). IR ($CHCl_3$): 3352*w*, 2994*w*, 2958*m*, 2913*w*, 2877*w*, 2173*w*, 1696*m*, 1623*w*, 1590*m*, 1506*s*, 1490*s*, 1461*s*, 1444*s*, 1411*s*, 1385*m*, 1267*s*, 1252*s*, 1157*m*, 1083*s*, 1003*m*, 873*m*, 846*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.19 (*s*, Me_3Si); 0.38–0.60 (*m*, $(MeCH_2)_3Si$); 0.83 (*t*, $J = 8.5$, $(MeCH_2)_3Si$); 1.38, 1.61 (2*s*, Me_2C); 7.51–7.70 (*m*, 3 arom. H); 7.93–8.00 (*m*, 2 arom. H); 8.86 (br. *s*, BzN*H*); 10.98 (br. *s*, H–N(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.9 (*s*, C=S); 165.8 (*s*, C=O); 152.7 (*s*, C(6)); 151.3 (*d*, C(2)); 138.2 (*s*, C(4)); 133.8 (*d*); 131.6 (*s*); 129.2 (2*d*); 127.7 (2*d*); 114.2 (*s*, Me_2C); 111.2 (*s*, C(5)); 103.5 (*s*, C(6′)); 91.3 (*s*, C(7′)); 90.1 (*d*, C(1′)); 89.5 (*d*, C(4′)); 82.4, 82.1 (2*d*, C(2′), C(3′)); 64.6 (*d*, C(5′)); 27.3, 25.7 (2*q*, Me_2C); 6.5 (*q*, $(MeCH_2)_3Si$); 4.6 (*t*, $(MeCH_2)_3Si$); −0.2 (*q*, Me_3Si). FAB-MS: 654 ($[M+1]^+$). Anal. calc. for $C_{31}H_{43}N_5O_5SSi_2$ (653.95): C 56.94, H 6.63, N 10.71; found: C 56.65, H 6.75, N 10.89.

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-8-iodoadenine* (**25**) *and* N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]-8-iodoadenine* (**26**). At 15°, a soln. of **16** (2.45 g, 4.56 mmol) and DCC (2.78 g, 13.47 mmol) in dry DMSO (13.5 ml) was treated dropwise with $Cl_2CHCOOH$ (0.19 ml, 2.30 mmol), stirred for 10 min, warmed to 25°, stirred for 90 min, and filtered. The residue was washed with small amounts of DMSO, and the combined filtrates were washed with hexane (4 × 40 ml). The DMSO layer was diluted with $CHCl_3$ (350 ml), washed with H_2O (2 × 100 ml), dried (Na_2SO_4), and evaporated, affording the crude aldehyde. At 0°, a soln. of EtMgBr (13.7 mmol) in THF (22.4 ml) was treated dropwise with (trimethylsilyl)acetylene (1.9 ml, 13.7 mmol), stirred for 10 min, warmed to 25°, stirred for 30 min, cooled to 0°, and treated with a soln. of the crude aldehyde in dry

THF (73 ml). The mixture was stirred for 3 h, treated with I_2 (5.22 g, 20.6 mmol), warmed to 25°, stirred for 1 h, and treated with sat. aq. NH_4Cl soln. (70 ml) and sat. aq. $Na_2S_2O_3$ soln. (60 ml). The org. layer was separated, and the aq. layer was extracted with AcOEt (2 × 70 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (250 g of silica gel; $CHCl_3$/AcOEt 5:2) gave crude **25** (542.7 mg, 19%), and crude **26** (566.9 mg, 20%).

Data of **25**: Yellow solid. R_f($CHCl_3$/AcOEt 5:2) 0.59.

Data of **26**: Yellow solid. R_f($CHCl_3$/AcOEt 5:2) 0.44.

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-8-iodoadenine* (**27**). At 25°, a soln. of crude **25** (542.7 mg) and imidazole (192.5 mg, 2.83 mmol) in dry DMF (17 ml) was treated dropwise with Et_3SiCl (0.43 ml, 2.56 mmol), stirred for 12 h, poured into ice-water (*ca.* 20 ml), and extracted with Et_2O/AcOEt 1:1 (4 × 10 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (23 g of silica gel; hexane/AcOEt 5:4) gave **27** (335.5 mg, 10% from **16**). Yellow solid. R_f(hexane/AcOEt 7:4) 0.49. M.p. 88°. $[\alpha]_D^{25} = -7.2$ ($c = 1.04$, $CHCl_3$). UV ($CHCl_3$): 290.0 (24000), 246.0 (17000). IR ($CHCl_3$): 3406*w*, 3008*m*, 2959*m*, 2877*w*, 2173*w*, 1711*m*, 1608*s*, 1588*m*, 1504*m*, 1486*m*, 1460*m*, 1423*s*, 1384*m*, 1356*w*, 1320*m*, 1269*m*, 1248*s*, 1160*m*, 1089*s*, 1004*m*, 846*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.09 (*s*, Me_3Si); 0.54–0.72 (*m*, (MeCH_2)$_3$Si); 0.95 (*t*, $J = 8.6$, (*Me*CH_2)$_3$Si); 1.41, 1.62 (2*s*, Me_2C); 7.48–7.65 (*m*, 3 arom. H); 7.96–8.04 (*m*, 2 arom. H); 9.05 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.4 (*d*, C(2)); 151.7 (*s*, C(6)); 148.3 (*s*, C(4)); 133.6 (*s*); 132.9 (*d*); 128.9 (2*d*); 127.8 (2*d*); 125.4 (*s*, C(5)); 114.0 (*s*, Me_2C); 105.2 (*s*, C(8)); 103.8 (*s*, C(6′)); 94.1 (*d*, C(1′)); 90.8 (*s*, C(7′)); 89.9 (*d*, C(4′)); 82.7 (*d*, C(2′)); 82.4 (*d*, C(3′)); 63.0 (*d*, C(5′)); 27.2, 25.4 (2*q*, Me_2C); 6.7 (*q*, (*Me*CH_2)$_3$Si); 4.8 (*t*, (MeCH_2)$_3$Si); −0.3 (*q*, Me_3Si). FAB-MS: 748 ([$M+1$]$^+$). Anal. calc. for $C_{31}H_{42}IN_5O_5Si_2$ (747.78): C 49.79, H 5.66, N 9.37; found: C 50.02, H 5.83, N 9.20.

Reaction of **27** *with Thiourea*. At 25°, a soln. of **27** (25.0 mg, 33.4 μmol) in PhMe (1.3 ml) was treated with thiourea (8.1 mg, 0.106 mmol), stirred at 60° for 35 min, and treated with sat. aq. $NaHCO_3$ soln. (0.90 ml) and sat. aq. $Na_2S_2O_3$ soln. (0.30 ml). The org. layer was separated, and the aq. layer was extracted with AcOEt (2 × 0.5 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (1.5 g of silica gel; hexane/AcOEt 2:1) gave **10** (5.4 mg, 26%) and **23** (13.4 mg, 61%).

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]-8-iodoadenine* (**28**). At 25°, a soln. of crude **26** (566.9 mg) and imidazole (196.7 mg, 2.89 mmol) in dry DMF (17 ml) was treated dropwise with Et_3SiCl (0.45 ml, 2.68 mmol), stirred for 11 h, poured into ice-water (*ca.* 30 ml), and extracted with Et_2O/AcOEt 1:1 (3 × 10 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (25 g of silica gel; hexane/AcOEt 5:4) gave **28** (260.3 mg, 8% from **16**). Light yellow solid. R_f(hexane/AcOEt 5:4) 0.50. M.p. 87°. $[\alpha]_D^{25} = -61.9$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 291.0 (24000), 245.0 (17000). IR ($CHCl_3$): 3406*w*, 3007*m*, 2959*m*, 2913*w*, 2877*w*, 2174*w*, 1711*s*, 1608*s*, 1588*s*, 1504*w*, 1486*m*, 1460*s*, 1422*s*, 1384*m*, 1315*m*, 1269*s*, 1248*s*, 1160*m*, 1089*s*, 1043*w*, 1004*m*, 892*w*, 846*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 1*; additionally, 0.19 (*s*, Me_3Si); 0.24–0.42 (*m*, (MeCH_2)$_3$Si); 0.75 (*t*, $J = 8.6$, (*Me*CH_2)$_3$Si); 1.41, 1.63 (2*s*, Me_2C); 7.48–7.65 (*m*, 3 arom. H); 7.96–8.05 (*m*, 2 arom. H); 8.98 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.3 (*s*, C=O); 152.5 (*d*, C(2)); 151.8 (*s*, C(6)); 148.3 (*s*, C(4)); 133.6 (*s*); 132.9 (*d*); 128.9 (2*d*); 127.8 (2*d*); 125.5 (*s*, C(5)); 114.2 (*s*, Me_2C); 104.9 (*s*, C(8)); 103.0 (*s*, C(6′)); 93.9 (*d*, C(1′)); 91.6 (*s*, C(7′)); 91.1 (*d*, C(4′)); 82.7 (*d*, C(2′)); 82.3 (*d*, C(3′)); 64.4 (*d*, C(5′)); 27.2, 25.5 (2*q*, Me_2C); 6.4 (*q*, (*Me*CH_2)$_3$Si); 4.4 (*t*, (MeCH_2)$_3$Si); −0.3 (*q*, Me_3Si). FAB-MS: 748 ([$M+1$]$^+$). Anal. calc. for $C_{31}H_{42}IN_5O_5Si_2$ (747.78): C 49.79, H 5.66, N 9.37; found: C 49.88, H 5.76, N 9.27.

Reaction of **28** *with Thiourea*. At 25°, a soln. of **28** (31.5 mg, 42.1 μmol) in PhMe (1.6 ml) was treated with thiourea (8.1 mg, 0.106 mmol), stirred at 60° for 35 min, and treated with sat. aq. $NaHCO_3$ soln. (0.70 ml) and sat. aq. $Na_2S_2O_3$ soln. (0.70 ml). The org. layer was separated, and the aq. layer was extracted with AcOEt (2 × 0.5 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (1.6 g of silica gel; hexane/AcOEt 2:1 → 1:2) gave **11** (10.0 mg, 38%) and **24** (14.7 mg, 53%).

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