Oligonucleosides with a Nucleobase-Including Backbone

Part 4

A Convergent Synthesis of Ethynediyl-Linked Adenosine Tetramers

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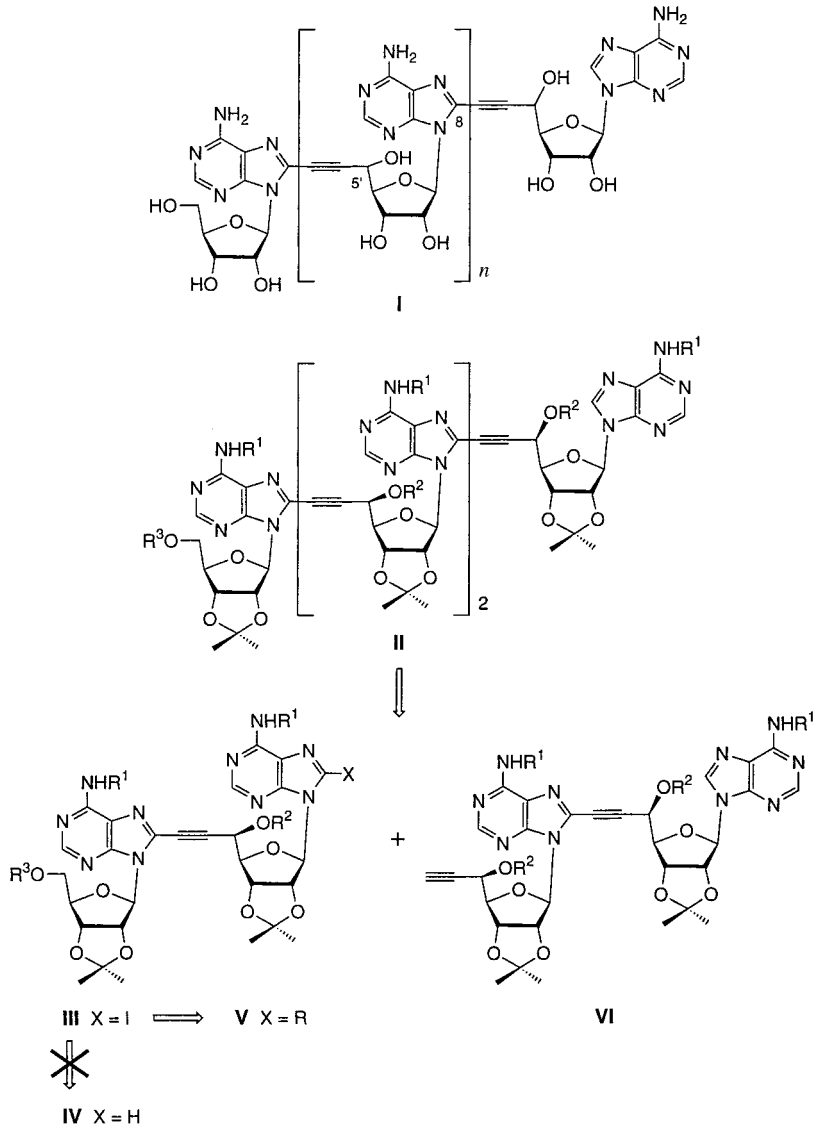
Deprotection of the tetramer **24**, obtained by coupling the iodinated dimer **18** with the alkyne **23** gave the 8′,5-ethynediyl-linked adenosine-derived tetramer **27** (*Scheme 3*). As direct iodination of C(5′)-ethynylated adenosine derivatives failed, we prepared **18** *via* the 8-amino derivative **17** that was available by coupling the imine **15** with the iodide **7**; **15**, in its turn, was obtained from the 8-chloro derivative **12** *via* the 4-methoxybenzylamine **14** (*Scheme 2*). This method for the introduction of the 8-iodo substituent was worked out with the *N*-benzoyladenosine **1** that was transformed into the azide **2** by lithiation and treatment with tosyl azide (*Scheme 1*). Reduction of **2** led to the amine **3** that was transformed into **7**. 1,3-Dipolar cycloaddition of **3** and (trimethylsilyl)acetylene gave **6**. The 8-substituted derivatives **4a**–**d** were prepared similarly to **2**, but could not be transformed into **7**. The known chloride **8** was transformed into the iodide **11** *via* the amines **9** and **10**. The amines **3**, **10**, and **16** form more or less completely persistent intramolecular C(8)N–H···O(5′) H-bonds, while the dimeric amine **17** forms a *ca*. 50% persistent H-bond. There is no UV evidence for a base-base interaction in the protected and deprotected dimers and tetramers.

1. Introduction. – In the context of the synthesis of 8,5′-ethynediyl-linked analogues of adenosine-oligonucleosides, we have so far prepared dimers (**I**, $n=0$; *Scheme 1*) by cross-coupling C(5′)-ethynylated and C(8)-halogenated monomers [1][2]. A convergent route appeared attractive for the preparation of higher oligomers that are required to test for base-pairing and formation of double-stranded associates. We planned to synthesise the tetramer **I** ($n=2$, *Scheme 1*) by cross-coupling dimers **III** and **VI** to **II**, followed by deprotection. Unfortunately, the method used to directly iodinate monomers at C(8), which is based on a regioselective lithiation at C(8) [1], failed for dimers of type **IV**. Treatment of **IV** ($R^1=Bz$, $R^2=R^3=Et_3Si$) with LDA at $-78°$ in THF led rapidly to a multitude of products, confirming the previously noted base-sensitivity of these ethynylated products [1]. The monomeric iodo derivatives had also been prepared by addition of (trimethylsilyl)ethynylmagnesium bromide to an iodo-aldehyde [1], but, in view of the base sensitivity of the ethynylated adenosines and the unsatisfactory diastereoselectivity of the addition, we required a different method to obtain dimeric iodides **III**, and considered to introduce a C(8)-substituent that is inert to the coupling conditions of the monomers (leading to **V**) and to subsequently displace it by an I substituent.

We describe the synthesis of two 8-I-substituted monomers (*Scheme 2*) and of the 8-iodinated dimer **18** (*Scheme 3*) by introducing a C(8)-imino group that is inert to the coupling conditions, and replacing it subsequently by a I substituent. We also describe the transformation of **18** into the protected 8,5′-ethynediyl-linked adenosine tetramer **24**, and its deprotection to **27** (*Scheme 4*).

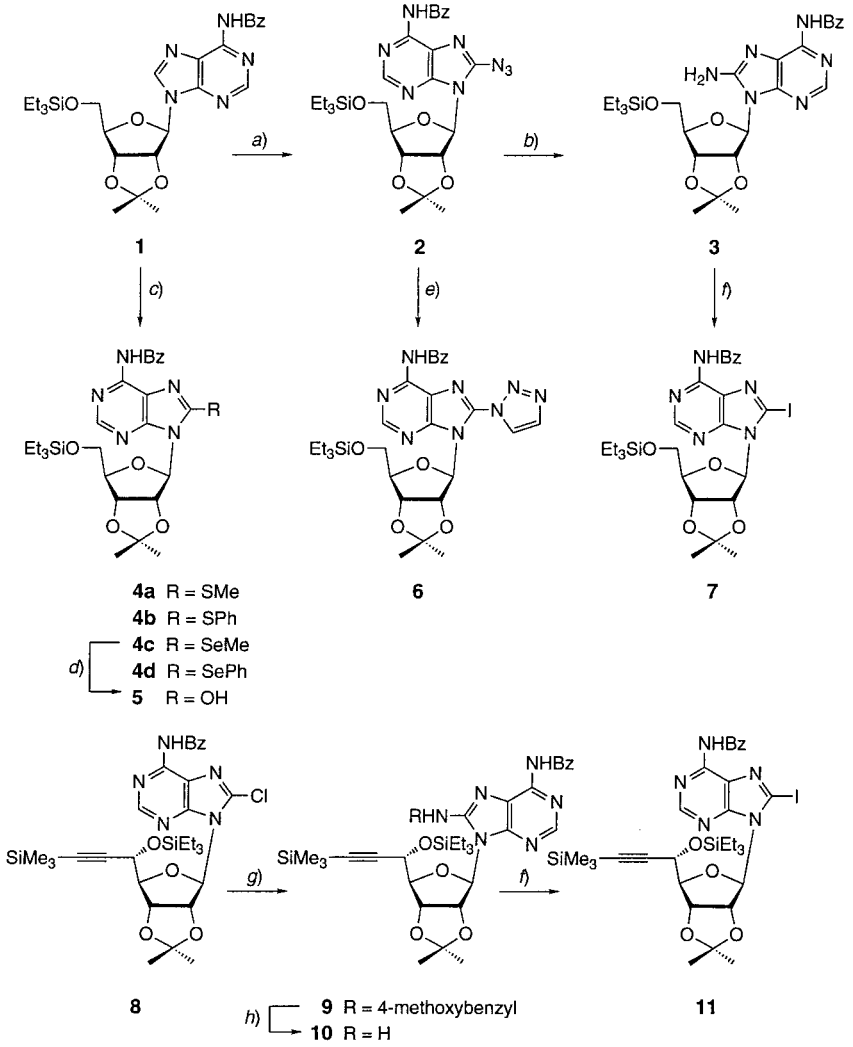
Scheme 1. *8,5′-Acetyleno-Linked Adenosine Oligomers* **I** *and Retrosynthetic Pathway for the Tetramer* **II**



Results and Discussion. – Several at C(8) N-, S-, and Se-substituted adenosines were considered as precursors of C(8)-iodo compounds. To evaluate these derivatives, we used the protected adenosine **1**, proceeding similarly as for the preparation of 8-Cl-adenosines [1], *i.e.*, by regioselective lithiation with LDA in THF, followed by treatment with the appropriate electrophile. Lithiation of **1** with LDA at $-78°$ followed by treatment with TsN_3 at $0°$ gave the 8-N_3 derivative **2** in 84% yield (*Scheme 2*), considerably improving the current method that is based on substitution of 8-Br derivatives with NaN_3 at $75-90°$ [3][4]. The monomers **4a–d** were similarly

prepared in yields of 46–94% by deprotonation of **1** with LDA and treatment with the appropriate S- or Se-electrophile. Oxidation of the methylseleno compound **4c** led to the 8-OH derivative **5**. Considering the potential of azides for the synthesis of heterocycles, we checked the reactivity of the azide **2** as a 1,3-dipolar reagent. While **2** reacted with (trimethylsilyl)acetylene to afford the triazole **6** in modest yields, it proved inert towards phenylacetylene, indicating the need for additional activation (appropriate substitution at N(6)?).

Scheme 2



a) LDA, TsN_3, THF; 84%. *b*) 10% Pd/C, H_2, EtOH; 91%. *c*) LDA, electrophile ($(MeS)_2$, $(PhS)_2$, $(MeSe)_2$, or PhSeCl), THF; **4a** (89%), **4b** (78%), **4c** (94%), **4d** (46%). *d*) *m*-Chloroperbenzoic acid, CH_2Cl_2; 96%. *e*) $Me_3Si-C\equiv CH$, DMF; 45%. *f*) $C_5H_{11}ONO$, KI, I_2, CH_2I_2; **7** (71%), **11** (82%). *g*) 4-Methoxybenzylamine, EtOH; 93%. *h*) DDQ, CH_2Cl_2/H_2O 18:1; 66% from **8**.

Attempts to introduce an 8-I substituent by treating compounds **2**, **4a**–**d**, and **6** with several sources of I anion failed. However, adoption of the known transformation of 6- and 2-aminopurines into the corresponding halides [5] proved successful. The amine **3** is available in a yield of 91% by hydrogenation of the azide **2**. Its treatment with amyl nitrite in the presence of KI and I_2 [6] in CH_2I_2 yielded 71% of the 8-I derivative **7** [1]. To test the scope of this iodination, we transformed the C(5′)-ethynylated 8-chloroadenosine derivative **8** [1] into the amine **10**. Treatment of **8** with 4-methoxybenzylamine [7–9] in EtOH afforded **9** that was debenzylated by DDQ in aqueous CH_2Cl_2 [10] to provide the amine **10** in an overall yield of 66%. Following the conditions described above, this amine was smoothly converted to the 8-iodo derivative **11** in 82% yield [1].

These results encouraged us to synthesize the key iodo dimer **18** *via* the amine **17** (*Scheme 3*). Desilylation of **12** (TBAF in THF) [1], followed by *O*-triethylsilylation, yielded 67% of the protected chloride **13**. Its treatment with 4-methoxybenzylamine gave the secondary amine **14** (95%). Oxidation of **14** with DDQ in aqueous CH_2Cl_2 led to a mixture of the imine **15** (18%) and the amine **16** (62%), while analogous oxidation of the *C*-trimethylsilylated **9** led only to the amine **10**[1]). The analogous oxidation of **14** under anhydrous conditions gave selectively the imine **15** (87%). Following the observation that the imine **15** is not stable to Et_3N, we prepared the amine **16** by exposing **15** for several hours to neat Et_3N. In view of this result and considering that anhydrous Et_3N had proven the best solvent for cross-coupling [2], we exposed **7** and **15** to the established cross-coupling conditions, and obtained the desired amino dimer **17** in 70%. The desired iodo dimer **18** was obtained in 55% yield from the amine **17**.

As described in the preceding paper [2], cross coupling of *N*-benzoylated acetylenoadenosines requires a temperature of 80°, while the analogous amines react at room temperature. We, therefore, prepared the dimeric amine **23** as the coupling partner for the iodide **18**. For this, we debenzoylated the known iodo derivative **19** [1] with 4-methoxybenzylamine in EtOH at 80°[2]) to **20** that was isolated in a yield of 81%. Coupling of **20** and **21** [1] proceeded smoothly at room temperature to give 85% of the dimer **22**, confirming the increased reactivity of the acetylenoadenosines with a free $H_2N-C(6)$ group. Cleavage of the $C-SiMe_3$ group of **22** was not straightforward. Treating **22** with $AgNO_3$ in aqueous THF/MeOH for 4.5 h, followed by addition of aqueous KCN [11][12] removed the Me_3Si group, but also led to partial cleavage of the Et_3SiO groups. Silylation of the crude with Et_3SiCl and imidazole in DMF was slow, but led to **23** in a yield of 72% from **22**, while silylation with triethylsilyl triflate gave a complex mixture, containing *N*-silylated products.

Since the iodo derivative **18** is insoluble in Et_3N, the dimers **18** and **23** were coupled in Et_3N/toluene 1:1 to yield 79% of the tetramer **24** (*Scheme 4*). This coupling proceeded smoothly at room temperature, but appreciably more slowly than the analogous coupling of the monomers, illustrating the reduced reactivity of the dimers **18** and **23**.

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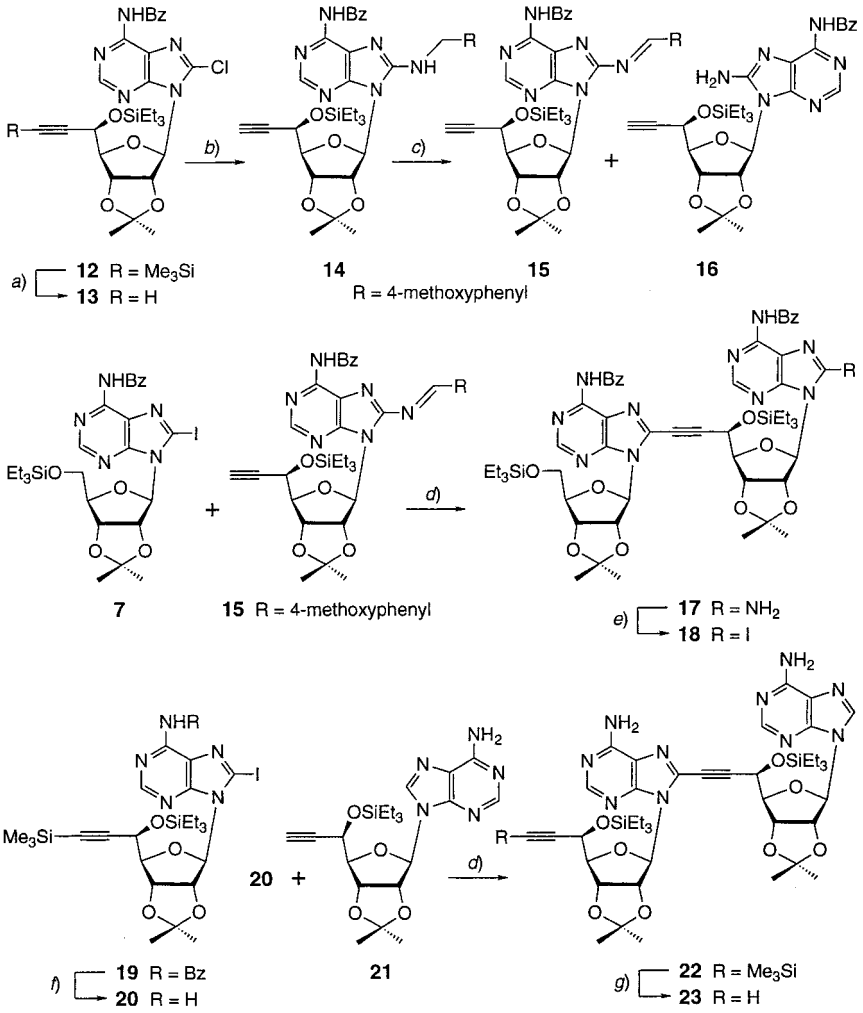
[1]) It is not clear whether this difference is due to the Me_3Si group or to the configuration at C(5′).

[2]) The conditions for this deprotection were discovered during an abortive attempt to introduce an NH_2 substituent at C(8).

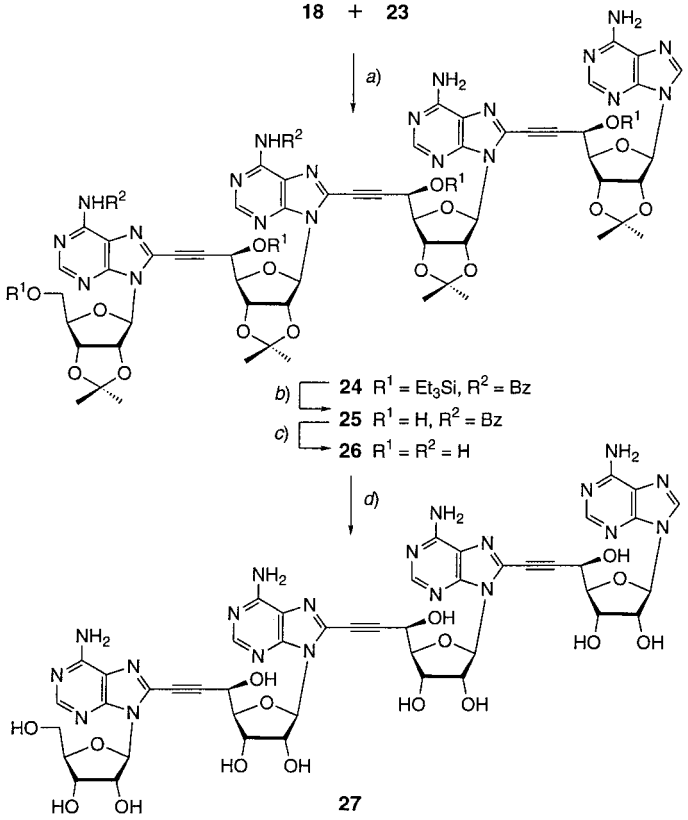
Scheme 3



a) Bu_4NF (TBAF), THF; Et_3SiCl, imidazole, DMF; 67%. *b*) 4-Methoxybenzylamine, EtOH; 95%. *c*) 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), CH_2Cl_2; **15** (87%) *or* DDQ, CH_2Cl_2/H_2O 18 : 1; **15** (18%), **16** (62%). *d*) CuI, $[Pd_2(dba)_3]$, $P(fur)_3$, Et_3N; **17** (70%), **22** (85%). *e*) $C_5H_{11}ONO$, KI, I_2, CH_2I_2; 55%. *f*) 4-Methoxybenzylamine, toluene; 81%. *g*) $AgNO_3$, THF/MeOH/H_2O; 5% aq. KCN; Et_3SiCl, imidazole, DMF; 72%.

The tetramer **24** was desilylated with aqueous AcOH to yield 89% of the tetrol **25**. Debenzoylation of **25** with aqueous NH_4OH in toluene/MeOH 1 : 1 afforded a complex mixture from which we isolated *ca.* 25% of the desired, slightly impure tetramine **26**, indicating that **25** and/or **26** are not stable to aqueous base. As HCOOH has proven effective for the deisopropylidenation of the related monomers [1] and dimers [2], we used it for the final deprotection of **26**. Treatment of **26** with 80% HCOOH at room

Scheme 4



a) CuI, $[Pd_2(dba)_3]$, $P(fur)_3$, Et_3N; 79%. *b*) THF/AcOH/H_2O 1:2:1; 89%. *c*) NH_4OH, toluene/MeOH/H_2O; 25%. *d*) HCO_2H/H_2O 4:1; 72%.

temperature for 22 h yielded the deprotected acetyleno-adenosine tetramer **27** in an overall yield of 16% from **24**.

A comparison of the ^{1}H-NMR data (*Tables 2* and *3* in the *Exper. Part*) shows that the 8-substituted monomers **2**, **4**–**6**, **13**, **15**, and **20** possess a flattened ring ($J(1',2') + J(3',4') = 4.8-6.3$ Hz [13]). The $(N) \rightleftharpoons (S)$ equilibrium is slightly shifted to the (N)-conformer ($J(1',2') = 1.8-2.5$ Hz, $J(3',4') = 3.0-3.8$ Hz), in agreement with the behaviour of the 8-halo analogues **7**, **11**, **12**, and **19** [1]. H–C(2′) of the sulfides **4a**–**b**, the selenides **4c**–**d**, the triazole **6**, and the halides **13** and **20** appears at a similar position as H–C(2′) of the halides **7**, **11**, **12**, and **19** (5.76–5.91 ppm), evidencing a complete *syn*-orientation of the nucleobase. The relatively weak upfield shift of H–C(2′) of the imine **15** (5.67 ppm), the azide **2** (5.66 ppm), and the alcohol **5** (5.56 ppm) indicates a dominant participation of the *syn*-conformer in the *syn* $\rightleftharpoons$ *anti* equilibrium. However, H–C(2′) of the primary amines **3**, **10**, and **16** is strongly shifted upfield and resonates at 5.06–5.27 ppm at a position similar to the H–C(2′) of the 8-unsubstituted adenosines **1** and **21**. These upfield shifts reveal an *anti*-conformation (see [1][2] and refs. cit. there) and

suggest a C(8)N–H···O(5′) H-bond, as it is known for related 8-aminopurines [14–16]. The intramolecular H-bond of **3**, **10**, and **16** is ascertained by a small $J(4',5')$ value of 1.8–3.5 Hz, evidencing a *trans*-arrangement of the H–C(4′) and the O–C(5′) bonds and, hence, a small distance between O(5′) and H_2N–C(8). Indeed, MM3* modeling of **3** (Macromodel V. 6.0, gas phase [17]) results in a bifurcated H-bond from HN–C(8) to O(5′) (H···O distance 1.75 Å) and O(4′) (H···O distance 2.24 Å), and in *synclinal* H–C(4′) and H–C(5′) bonds (calculated $J(4',5')$ values of 0.8 and 3.5 Hz, resp.). Due to this H-bond, the amines **3**, **10**, and **16** show an enhanced ring puckering ($J(1',2') + J(3',4') = 7.3–8.3$ Hz) and a *ca.* 1:1 (*N*) ⇌ (*S*) equilibrium. The larger $J(3',4')$ value and the stronger downfield shift of H–C(2′) of the D-*allo*-configured **16** as compared to the corresponding values of the D-*ribo*-configured **3** and L-*talo*-configured **10** ($\Delta J \approx 1$ Hz, $\Delta\delta \approx 0.2$ ppm) indicate a *ca.* 80% preference of **16** for the intramolecular H-bond and the *syn*-conformation. Monoalkylation at H_2N–C(8) of **10** and **16** leads to a destabilisation of the intramolecular H-bond. Again, the D-*allo*-configured **14** shows a weaker preference for the intramolecular H-bond than the L-*talo*-configured **9**: 45 *vs.* 60%, as calculated from $J(4',5') = 5.5$ and 4.5 Hz, respectively. In agreement with this assignment, H–C(2′) of **14** resonates 0.2 ppm downfield to H–C(2′) of **9**.

H–C(2′/II)[3]) of the dimers **17**, **18**, **22**, and **23** resonates at 5.61–5.70 ppm (*Table 4*, *Exper. Part*) indicating a complete preference for the *syn*-conformation. H–C(2′/I) of these dimers shows only a weak upfield shift ($\Delta\delta = 0.04–0.07$ ppm relative to δ(H–C(2′/II)). Neglecting the influence of the ethynyl group on δ(H–C(2′/II)), this weak upfield shift suggests a more or less complete preference for the *syn*-conformation of unit I of the iodo derivative **18**, the 8-unsubstituted **22** and **23**, and, surprisingly, also of the amine **17**. However, $J(4',5'/I)$ of the amine **17** (5.5 Hz) is distinctly smaller than $J(4',5'/I)$ of **18** (8.0 Hz) and reveals a *ca.* 45% persistent intramolecular H-bond and thus a *ca.* 11:9 *syn* ⇌ *anti* equilibrium. Similarly, the smaller $J(4',5'/I)$ values of **22** (7.5 Hz) and **23** (7.0 Hz) reflect a weaker steric interaction of the nucleobase with the propargylic side chain in the *anti*-conformation (compare with $J(4',5') = 4.8$ Hz of **21** [2]; *Table 3*) and indicate a 7:3 and a 6:4 *syn* ⇌ *anti* equilibrium, respectively. Thus, there is a significant influence of the 8-ethynyl group on δ(H–C(2′)). The $J(4',5'/II–IV)$ values of the protected tetramer **24** are large and evidence a *syn*-conformation for units II–IV, whereas $J(4',5'/I) = 7.5$ Hz indicates a 7:3 *syn* ⇌ *anti* equilibrium, as already observed for the dimer **22**.

2′,3′-*O*-Isopropylidenated 5′-hydroxyadenosines form a completely persistent intramolecular O(5′)–H···N(3) H-bond in $CDCl_3$ [1]. In (D_6)DMSO solution, the persistence of such a H-bond is *ca.* 20% [19]. Thus, the tetrols **25** and **26** may form weakly persistent intramolecular H-bonds. $J(5',OH)$ values of 5–6 Hz suggest more or less completely solvated OH groups (see [20] and refs. cit. there). However, the $J(4',5'/I–IV)$ values of **25** and **26** are smaller than the corresponding values of the protected **24** (*Table 4*, *Exper. Part*). They suggest 10–30% persistent intramolecular H-bonds, which are also evidenced by a downfield shift of the OH signals; the primary HO–C(5′/IV) of **25** and **26** resonate at 4.92 and 5.24 ppm, respectively, and the secondary HO–C(5′/I–III) at 6.59–6.78 ppm.

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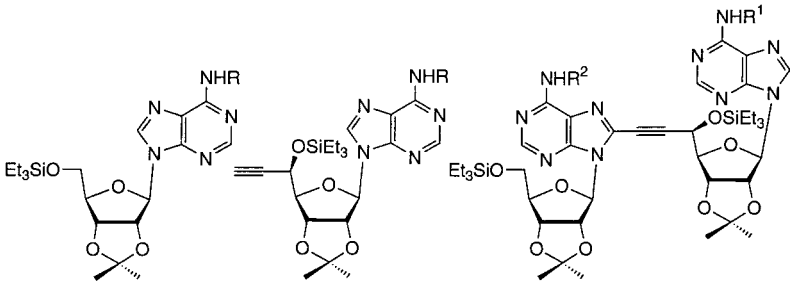
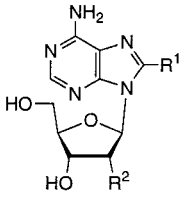
[3]) Starting from the downstream end, the units of the oligonucleosides are specified by roman numerals (*cf.* [18]).



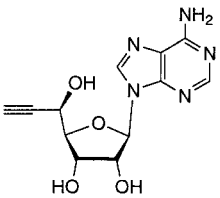
1 R = Bz
28 R = H

29 R = Bz
21 R = H

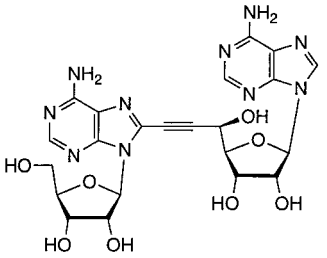
30 $R^2 = R^1 = Bz$
31 $R^2 = Bz$, $R^1 = H$
32 $R^2 = H$, $R^1 = Bz$
33 $R^2 = R^1 = H$



34 $R^1 = H$, $R^2 = OH$
35 $R^1 = C{\equiv}CH$, $R^2 = OH$
36 $R^1 = C{\equiv}CH$, $R^2 = H$



37



38

To assess interactions between the base units, we compared the UV spectra of the tetramers **24** ($CHCl_3$) and **27** (DMSO) with those of the related dimers and monomers (*Table 1*). We first checked for a possible influence of the ethynyl substituent at C(5′) by comparing the UV spectra of the protected adenosines **28** and **21**, the corresponding benzoates **1** and **29**, and the unprotected adenosines **34** and **37**. As expected, there is no evidence for such an interaction; the difference of 6 nm for λ_{max} of **34** and **37** is due to the solvent. The UV spectra of 8-ethynyladenosine (**35** [22]) and 2′-deoxy-8-ethynyladenosine (**36** [23]) show in H_2O a band with $\lambda_{max} = 292$ nm. Besides this band, the UV spectrum of **36** shows a shoulder at 303 nm. This shoulder is found in the UV spectra of a series of 8-(alk-1-ynyl)adenosines [23] [24]; it is characteristic for 8-ethynyladenosines. On the basis of a solvent correction of 6 nm for the 8-unsubstituted and for the 8-ethynyl-substituted adenine moiety of **38** in DMSO, one expects bands at 266 and 298 nm and a shoulder at 309 nm, close to the observed bands at 271 and 301 nm, and a shoulder at 312 nm. The maximum at 271 nm does not correctly reflect the λ_{max} of the 8-unsubstituted adenine moiety as it is also influenced by strong absorptions of the 8-ethynyladenine moiety. The λ values of 301 and 312 nm probably indicate a larger solvent shift (9 instead of 6 nm) for the 8-ethynyladenine moiety. Thus, there is no evidence for a base/base interaction in **38**. The UV spectrum of the tetramer **27** resembles that of the dimer **38**, again in keeping with the absence of a base/base interaction. The protected monoamines **28** and **21** show exactly the same λ_{max} as adenosine (**34**), suggesting that the bands of the protected diamine **33** should show a hypsochromic shift of *ca.* 6 nm (*i.e.*, a solvent shift for the change from H_2O to DMSO)

to the bands of the deprotected diamine **38**. This is indeed the case ($\Delta\lambda = 4-6$ nm); there is no evidence for a base/base interaction in **33**.

Table 1. *UV Absorptions of the Monomers* **1**, **21**, **28**, **29**, *and* **34**–**37**, *the Dimers* **30**–**33**, *and* **38**, *and the Tetramers* **24** *and* **27**

Compound Solvent	**1** [1] $CHCl_3$	**28** [2] $CHCl_3$	**29** [1] $CHCl_3$	**21** [2] $CHCl_3$	**30** [2] $CHCl_3$
λ_{max} [nm] (ε)	282 (14500)[a]), 276 (15000), 249 (9500)	260 (14000)	279 (19000), 247 (11000)[a])	260 (13000)	317 (22500), 304 (35000), 292 (39000), 250 (29000)
Compound Solvent	**31** [2] $CHCl_3$	**32** [2] $CHCl_3$	**33** [2] $CHCl_3$	**24** $CHCl_3$	**34** [21] H_2O (pH 7)
λ_{max} [nm] (ε)	317 (23500), 305 (32000), 298 (31000), 253 (29000)	308 (16500)[a]), 284 (32000), 248 (13000)	308 (15500)[a]), 295 (20000), 266 (21000)	316 (61000)[a]), 304 (71000), 296 (71000), 251 (55000)	260 (14400)
Compound Solvent	**35** [22] H_2O	**36** [23] H_2O	**37** [1] DMSO	**38** [2] DMSO	**27** DMSO
λ_{max} [nm] (ε)	292 (17000)	303 (13000)[a]), 292 (16800)	266 (13000)	312 (13500)[a]), 301 (17000), 271 (17000)	311 (29500)[a]), 301 (48000), 278 (28000), 270 (25500)

[a]) Shoulder.

The situation is more complicated for the protected tetramer **24**. Three units can be distinguished, *viz*. the 8-unsubstituted adenine (unit I), the 8-ethynylated adenine (unit II), and the 8-ethynylated *N*-benzoyladenine (units III and IV). We considered the monomers **1**, **28**, **29**, and **21**, and the dimers **33**, **31**, and **30** as models to assess the interactions between the nucleobases of units I/II, II/III, and III/IV of **24**. The comparison of the UV spectra of **28** and **1**, and of **21** and **29** shows that *N*-benzoylation leads to a new band (for the benzamido moiety) at *ca*. 250 nm and to a bathochromic shift of *ca*. 20 nm of the band for the adenine moiety. The analysis is impaired by the broad bands of the N^6-benzoyladenines. A comparison of the UV spectra of the dibenzamide **30** and the monobenzamides **1** and **29** shows the expected bathochromic shift for the 8-ethynyladenine moiety (25 nm) and a band at 317 nm instead of the expected shoulder. Again, the strong band of the 8-ethynyladenine moiety prevents an exact assignment of λ_{max} of the 8-unsubstituted adenine moiety. The UV spectrum of the monobenzamide **31** resembles that of the dibenzamide **30**, and that of the monobenzamide **32** resembles that of the diamine **33** (apart from the band for the benzamido group at 248 nm), evidencing the dominant contribution of the 8-ethynyladenine moiety. The UV spectrum of the tetramer **24** is expected to closely resemble the spectra of **30** and **31**; this is indeed the case, again in agreement with the absence of any base/base interaction.

We thank Dr. *B. Bernet* for his analytical contributions, and the *Swiss National Science Foundation*, *F. Hoffmann-La Roche AG*, Basel, and *Givaudan AG*, Dübendorf, for generous support.

Experimental Part

General. See [1].

*8-Azido-*N^6*-benzoyl-2′,3′-*O*-isopropylidene-5′-*O*-(triethylsilyl)adenosine* (**2**). A soln. of ^{i}Pr$_2$NH (63 µl, 0.45 mmol) in dry THF (1.4 ml) was cooled to 0°, treated dropwise with 1.6M BuLi in hexane (0.28 ml, 0.45 mmol), stirred for 25 min, cooled to −78°, treated dropwise with a soln. of **1** [1] (94.2 mg, 0.18 mmol) in dry THF (1.4 ml), stirred for 3 h, treated with TsN_3 (111 mg, 0.56 mmol), stirred for 15 min, warmed to 0°, stirred for 1 h, and treated with sat. aq. NH_4Cl soln. (2.0 ml) and H_2O (1.0 ml). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 1.0 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (5.0 g of silica gel; $CHCl_3$/AcOEt 5:1) gave **2** (85.1 mg, 84%). Light orange plates. R_f (hexane/AcOEt 1:1) 0.57. M.p. 114°. $[\alpha]_D^{25} = -25.9$ ($c = 1.06$, $CHCl_3$). UV ($CHCl_3$): 302 (20000), 251 (18000). IR ($CHCl_3$): 3408*w*, 2997*w*, 2957*w*, 2913*w*, 2877*w*, 2156*s*, 1708*m*, 1615*s*, 1589*m*, 1517*w*, 1498*w*, 1478*m*, 1457*s*, 1431*m*, 1376*s*, 1328*w*, 1268*m*, 1159*w*, 1090*s*, 1004*w*, 972*w*, 946*w*, 916*w*, 898*w*, 868*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.52 (*q*, $J = 7.9$, (MeCH_2)$_3$Si); 0.89 (*t*, $J = 7.9$, (*Me*CH$_2$)$_3$Si); 1.40, 1.61 (2*s*, Me$_2$C); 7.49–7.58 (*m*, 2 arom. H); 7.58–7.65 (*m*, 1 arom. H); 7.96–8.03 (*m*, 2 arom. H); 8.78 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 151.8 (*s*, C(6)); 151.5 (*d*, C(2)); 148.3 (*s*, C(4)); 144.1 (*s*, C(8)); 133.8 (*s*); 132.8 (*d*); 129.0 (2*d*); 127.8 (2*d*); 121.5 (*s*, C(5)); 114.3 (*s*, Me$_2$*C*); 89.1 (*d*, C(1′)); 87.8 (*d*, C(4′)); 82.7 (*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: 567 ([$M+1$]$^+$). Anal. calc. for $C_{26}H_{34}N_8O_5Si$ (566.69): C 55.11, H 6.05, N 19.77; found: C 54.92, H 5.86, N 19.68.

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the C(8)-Substituted Adenosines* **1**–**7** *in $CDCl_3$ Solution*

	1 [1]	**2**	**3**	**4a**	**4b**	**4c**	**4d**	**5**	**6a**[a])	**7** [1]
H–C(2)	8.83	8.69	8.55	8.67	8.75	8.68	8.76	8.40	8.81	8.73
H–C(1′)	6.25	6.04	6.41	6.09	6.33	6.09	6.33	6.28	6.75	6.14
H–C(2′)	5.26	5.66	5.06	5.76	5.77	5.79	5.77	5.56	5.91	5.81
H–C(3′)	4.95	5.10	4.97	5.13	5.15	5.12	5.13	5.01	5.20	5.18
H–C(4′)	4.45	4.27	4.24	4.29	4.31	4.33	4.29	4.27	4.23	4.32
H_a–C(5′)	3.75	3.66	3.87	3.66	3.70	3.66	3.69	3.76	3.68	3.65
H_b–C(5′)	3.87	3.77	4.00	3.76	3.82	3.77	3.80	3.84	3.78	3.76
J(1′,2′)	2.7	2.3	3.8	2.2	2.5	2.2	2.5	2.2	1.8	2.3
J(2′,3′)	6.0	6.5	6.7	6.5	6.5	6.5	6.5	6.5	6.5	6.3
J(3′,4′)	2.5	3.5	4.3	3.5	3.8	3.5	3.5	3.5	3.8	3.5
J(4′a,5′)	4.0	6.5	1.8	6.5	6.5	6.5	6.5	6.5	7.0	6.5
J(4′b,5′)	3.7	6.5	2.2	6.5	6.5	6.5	6.5	6.5	7.0	6.5
J(5′a,5′b)	11.0	10.8	10.8	10.8	10.8	10.8	10.8	10.5	10.8	10.5

[a]) In CD_3OD.

*8-Amino-*N^6*-benzoyl-2′,3′-*O*-isopropylidene-5′-*O*-(triethylsilyl)adenosine* (**3**). At 25°, a soln. of **2** (535.5 mg, 0.945 mmol) in EtOH (21 ml) was treated with 10% Pd/C (544.0 mg), stirred for 4 h under H_2, treated with Ar stream, filtered, and evaporated. FC (20 g of silica gel; $CHCl_3$/AcOEt 1:2) gave **3** (464.4 mg, 91%). White solid. R_f ($CHCl_3$/acetone 3:1) 0.50. M.p. 174°. $[\alpha]_D^{25} = -6.5$ ($c = 1.07$, $CHCl_3$). UV ($CHCl_3$): 303 (16000), 246 (14000). IR ($CHCl_3$): 3467*w*, 3408*w*, 3324*w*, 2998*w*, 2960*m*, 2914*w*, 2878*w*, 1700*m*, 1639*s*, 1612*m*, 1590*w*, 1554*w*, 1500*m*, 1481*m*, 1438*s*, 1417*w*, 1387*m*, 1334*w*, 1255*m*, 1172*w*, 1156*w*, 1129*w*, 1107*m*, 1084*m*, 1048*w*, 1026*w*, 973*w*, 935*w*, 897*w*, 859*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.65 (*q*, $J = 7.9$, (MeCH_2)$_3$Si); 0.99 (*t*, $J = 7.9$, (*Me*CH$_2$)$_3$Si); 1.37, 1.64 (2*s*, Me$_2$C); 5.75 (br. *s*, NH$_2$); 7.44–7.53 (*m*, 2 arom. H); 7.54–7.62 (*m*, 1 arom. H); 7.95–8.03 (*m*, 2 arom. H); 8.59 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.0 (*s*, C=O); 153.1 (*s*, C(6)); 153.0 (*d*, C(2)); 149.2 (*s*, C(4)); 144.2 (*s*, C(8)); 133.8 (*s*); 132.3 (*d*); 128.6 (2*d*); 127.9 (2*d*); 122.9 (*s*, C(5)); 115.2 (*s*, Me$_2$*C*); 88.2 (*d*, C(1′)); 84.6 (*d*, C(4′)); 82.9 (*d*, C(2′)); 79.3 (*d*, C(3′)); 61.8 (*t*, C(5′)); 27.4, 25.4 (2*q*, *Me*$_2$C); 6.6 (*q*, (*Me*CH$_2$)$_3$Si); 4.0 (*t*, (MeCH$_2$)$_3$Si). FAB-MS: 541 ([$M+1$]$^+$). Anal. calc. for $C_{26}H_{36}N_6O_5Si$ (540.69): C 57.76, H 6.71, N 15.54; found: C 57.84, H 6.85, N 15.68.

Iodination of **3**. At 25°, a suspension of **3** (23.1 mg, 42.7 µmol) in CH_2I_2 (0.35 ml) was treated with $C_5H_{11}ONO$ (0.12 ml, 0.854 mmol), KI (21.3 mg, 0.128 mmol), and I_2 (35.1 mg, 0.138 mmol), warmed to 55°,

stirred for 2 h, diluted with $CHCl_3$ (2.0 ml), washed with sat. aq. $Na_2S_2O_3$ soln. (0.5 ml) and brine (0.5 ml), dried (Na_2SO_4), and evaporated. FC (1.5 g of silica gel; hexane/AcOEt 5:4) gave **7** [1] (19.7 mg, 71%).

General Procedure for the Preparation of **4a–d**. Similarly to the preparation of **2**, **1** was treated with LDA and 3 equiv. of the electrophile ($(MeS)_2$, $(PhS)_2$, $(MeSe)_2$, or PhSeCl), followed by normal workup.

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-(methylthio)-5′*-O-*(triethylsilyl)adenosine* (**4a**). 89% Yield. Light yellow solid. R_f (hexane/AcOEt 1:1) 0.41. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 2*; additionally, 0.50 (*q*, *J* = 7.9, $(MeCH_2)_3Si$); 0.88 (*t*, *J* = 7.9, $(MeCH_2)_3Si$); 1.40, 1.61 (2*s*, Me_2C); 2.77 (*s*, MeS); 7.46–7.65 (*m*, 3 arom. H); 7.94–8.03 (*m*, 2 arom. H); 8.92 (br. *s*, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): 164.1 (*s*, C=O); 154.8 (*s*, C(6)); 152.9 (*s*, C(4)); 150.8 (*d*, C(2)); 146.4 (*s*, C(8)); 133.7 (*s*); 132.2 (*d*); 128.5 (2*d*); 127.3 (2*d*); 122.8 (*s*, C(5)); 113.8 (*s*, Me_2C); 89.8 (*d*, C(1′)); 87.4 (*d*, C(4′)); 82.4 (*d*, C(2′)); 81.6 (*d*, C(3′)); 62.3 (*t*, C(5′)); 26.8, 25.0 (2*q*, Me_2C); 14.3 (*q*, MeS); 6.1 (*q*, $(MeCH_2)_3Si$); 3.8 (*t*, $(MeCH_2)_3Si$).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-(phenylthio)-5′*-O-*(triethylsilyl)adenosine* (**4b**). 78% Yield. Light yellow solid. R_f (hexane/AcOEt 5:4) 0.44. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 2*; additionally, 0.53 (*q*, *J* = 7.9, $(MeCH_2)_3Si$); 0.90 (*t*, *J* = 7.9, $(MeCH_2)_3Si$); 1.41, 1.62 (2*s*, Me_2C); 7.30–7.61 (*m*, 8 arom. H); 7.83–7.91 (*m*, 2 arom. H); 9.14 (br. *s*, NH).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-(methylseleno)-5′*-O-*(triethylsilyl)adenosine* (**4c**). 94% Yield. White solid. R_f (hexane/AcOEt 5:4) 0.38. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 2*; additionally, 0.51 (*q*, *J* = 8.0, $(MeCH_2)_3Si$); 0.88 (*t*, *J* = 8.0, $(MeCH_2)_3Si$); 1.41, 1.62 (2*s*, Me_2C); 2.67 (*s*, MeSe); 7.45–7.65 (*m*, 3 arom. H); 7.96–8.06 (*m*, 2 arom. H); 8.97 (br. *s*, NH).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-(phenylseleno)-5′*-O-*(triethylsilyl)adenosine* (**4d**). 46% Yield. Yellow solid. R_f (hexane/AcOEt 2:1) 0.42. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 2*; additionally, 0.51 (*q*, *J* = 8.0, $(MeCH_2)_3Si$); 0.88 (*t*, *J* = 8.0, $(MeCH_2)_3Si$); 1.40, 1.61 (2*s*, Me_2C); 7.31–7.40 (*m*, 3 arom. H); 7.45–7.52 (*m*, 2 arom. H); 7.55–7.62 (*m*, 1 arom. H); 7.66–7.71 (*m*, 2 arom. H); 7.90–7.96 (*m*, 2 arom. H); 9.13 (br. *s*, NH).

N^6-*Benzoyl-8-hydroxy-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**5**). At 25°, a soln. of **4c** (90.8 mg, 0.15 mmol) in dry CH_2Cl_2 (2.7 ml) was treated with *m*-chloroperbenzoic acid (52.2 mg, 0.3 mmol), stirred for 1 h, washed with sat. aq. $NaHCO_3$ soln. (2.0 ml) and brine (1.0 ml), dried (Na_2SO_4), and evaporated. FC (3.0 g of silica gel; hexane/AcOEt 2:1) gave **5** (76.4 mg, 96%). White solid. R_f (hexane/AcOEt 2:1) 0.48. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 2*; additionally, 0.60 (*q*, *J* = 8.0, $(MeCH_2)_3Si$); 0.96 (*t*, *J* = 8.0, $(MeCH_2)_3Si$); 1.40, 1.61 (2*s*, Me_2C); 7.49–7.60 (*m*, 2 arom. H); 7.60–7.72 (*m*, 1 arom. H); 7.96–8.03 (*m*, 2 arom. H); 8.89 (br. *s*, NH); 9.57 (br. *s*, OH).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-(*1H-*[1,2,3]triazol-1-yl)-5′*-O-*(triethylsilyl)adenosine* (**6**). At 25°, a soln. of **2** (20.1 mg, 35.5 μmol) in dry DMF (0.6 ml) was treated with (trimethylsilyl)acetylene (40 μl, 0.28 mmol), stirred for 20 h at 80°, poured into ice-water (*ca.* 4 ml), and extracted with Et_2O/AcOEt 1:1 (3 × 1.0 ml). The combined org. layers were washed with H_2O, dried (Na_2SO_4), and evaporated. FC (1.5 g of silica gel; CH_3Cl/AcOEt 7:2) gave **6** (9.4 mg, 45%). Green solid. R_f (CH_3Cl/AcOEt 7:2) 0.43. ^{1}H-NMR (200 MHz, CD_3OD): see *Table 2*; additionally, 0.48 (*q*, *J* = 8.0, $(MeCH_2)_3Si$); 0.86 (*t*, *J* = 8.0, $(MeCH_2)_3Si$); 1.40, 1.59 (2*s*, Me_2C); 7.50–7.61 (*m*, 2 arom. H); 7.61–7.72 (*m*, 1 arom. H); 8.01, 8.83 (2*d*, *J* = 1.3, $C_2H_2N_3$); 8.02–8.09 (*m*, 2 arom. H).

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]-8-{[(4-methoxyphenyl)methyl]amino}adenine* (**9**). At 25°, a soln. of **8** [1] (343.2 mg, 0.52 mmol) in dry EtOH (10.0 ml) was treated with 4-methoxybenzylamine (0.20 ml, 1.57 mmol), stirred for 25 h, and evaporated. The residue was dissolved in $CHCl_3$ (18 ml), washed with sat. aq. $NaHCO_3$ soln. (5.0 ml) and brine (5.0 ml), and dried (Na_2SO_4). Evaporation and FC (20 g of silica gel; hexane/AcOEt 5:7) gave **9** (366.4 mg, 93%), which contained traces of impurities. White solid. R_f (hexane/AcOEt 1:1) 0.44. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 0.17 (*s*, Me_3Si); 0.52 (*q*, *J* = 8.2), 0.53 (*q*, *J* = 8.0) ($(MeCH_2)_3Si$); 0.85 (*t*, *J* = 8.1, $(MeCH_2)_3Si$); 1.42, 1.64 (2*s*, Me_2C); 3.79 (*s*, MeO); 4.56 (*dd*, *J* = 15.0, 4.0), 4.77 (*dd*, *J* = 15.0, 7.0) ($ArCH_2$); 6.04 (*dd*, *J* = 7.0, 4.0, HN–C(8)); 6.87 (*d*, *J* = 8.5, 2 arom. H); 7.30 (*d*, *J* = 8.5, 2 arom. H); 7.43–7.60 (*m*, 3 arom. H); 7.93–8.02 (*m*, 2 arom. H); 8.81 (br. *s*, HN–C(6)).

*8-Amino-*N^6-*benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]adenine* (**10**). At 25°, a soln. of **9** (366.4 mg, *ca.* 0.48 mmol) in CH_2Cl_2/H_2O 18:1 (12.8 ml) was treated with DDQ (150.9 mg, 0.665 mmol), stirred for 5 h, diluted with $CHCl_3$ (40 ml), washed with sat. aq. $NaHCO_3$ soln. (15 ml) and brine (15 ml), dried (Na_2SO_4), and evaporated. FC (26 g of silica gel; $CHCl_3$/acetone 3:1) gave **10** (119.6 mg, 66% from **8**). Light pink solid. R_f ($CHCl_3$/AcOEt 1:3) 0.60. M.p. 113°. $[\alpha]_D^{25} = +8.6$ (*c* = 1.02, $CHCl_3$). UV ($CHCl_3$): 303 (17000), 244 (15000). IR ($CHCl_3$): 3464*w*, 3330*w*, 2997*w*, 2960*m*, 2914*w*, 2878*w*, 2176*w*, 1700*m*, 1638*s*, 1612*m*, 1584*w*, 1553*w*, 1500*m*, 1481*m*, 1438*s*, 1418*w*, 1387*m*, 1328*w*, 1304*w*, 1156*w*, 1125*m*, 1088*s*, 1018*w*, 969*w*, 942*w*, 847*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 0.15 (*s*, Me_3Si); 0.57–

Table 3. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the C(8)-Substituted Hept-6-ynofuranosyladenines* **9**–**16** *and* **19**–**21** *in $CDCl_3$ Solution*

	9	**10**	**11** [1]	**12** [1]	**13**	**14**	**15**	**16**	**19** [1]	**20**	**21** [2]
H–C(2)	8.60	8.52	8.76	8.77	8.76	8.59	8.75	8.55	8.73	8.21	8.36
H–C(1′)	6.13	6.36	6.15	6.24	6.25	6.06	6.76	6.32	6.13	6.07	6.18
H–C(2′)	5.59	5.07	5.77	5.85	5.78	5.81	5.67	5.27	5.90	5.88	5.25
H–C(3′)	4.95	4.85	5.29	5.24	5.27	4.96	5.34	5.09	5.26	5.24	5.12
H–C(4′)	4.30	4.25	4.22	4.22	4.26	4.23	4.27	4.26	4.22	4.19	4.39
H–C(5′)	4.49	4.66	4.41	4.43	4.55	4.41	4.67	4.71	4.41	4.39	4.63
H–C(7′)	–	–	–	–	2.35	2.10	2.29	2.61	–	–	2.48
J(1′,2′)	3.7	4.5	2.0	2.0	2.0	3.0	2.0	3.8	2.0	1.8	3.0
J(2′,3′)	6.5	6.5	6.5	6.3	6.5	6.8	6.3	6.5	6.0	6.5	6.5
J(3′,4′)	3.0	3.8	3.0	2.8	3.3	3.0	3.5	3.5	2.8	3.0	2.5
J(4′,5′)	4.5	2.5	8.0	7.5	7.8	5.5	8.0	3.5	8.0	8.8	4.8
J(5′,7′)	–	–	–	–	2.2	2.2	2.2	2.2	–	–	2.2

0.79 (*m*, (MeC*H*$_2$)$_3$Si); 0.98 (*t*, *J* = 8.1, (*Me*CH$_2$)$_3$Si); 1.35, 1.64 (2*s*, Me$_2$C); 5.80 (br. *s*, NH$_2$); 7.44 (br. *t*, *J* ≈ 7.8, 2 arom. H); 7.54 (br. *t*, *J* ≈ 7.8, 1 arom. H); 7.96 (br. *t*, *J* ≈ 7.8, 2 arom. H); 8.95 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.9 (*s*, C=O); 153.3 (*d*, C(2)); 153.0 (*s*, C(6)); 149.2 (*s*, C(4)); 144.2 (*s*, C(8)); 133.8 (*s*); 132.3 (*d*); 128.6 (2*d*); 127.9 (2*d*); 122.9 (*s*, C(5)); 115.4 (*s*, Me$_2$*C*); 102.5 (*s*, C(6′)); 91.7 (*s*, C(7′)); 88.2 (*d*, C(1′)); 86.2 (*d*, C(4′)); 82.0 (*d*, C(2′)); 80.0 (*d*, C(3′)); 63.0 (*d*, C(5′)); 27.4, 25.5 (2*q*, *Me*$_2$C); 6.7 (*q*, (*Me*CH$_2$)$_3$Si); 4.5 (*t*, (MeCH$_2$)$_3$Si); −0.4 (*q*, Me$_3$Si). FAB-MS: 637 ([*M* + 1]$^+$). Anal. calc. for $C_{31}H_{44}N_6O_5Si_2$ (636.90): C 58.46, H 6.96, N 13.20; found: C 58.50, H 6.99, N 13.13.

Iodination of **10**. At 25°, a suspension of **10** (12.3 mg, 19.7 μmol) in CH_2I_2 (0.18 ml) was treated with $C_5H_{11}ONO$ (8.0 μl, 59.2 μmol), KI (38.7 mg, 0.233 mmol) and I_2 (61.8 mg, 0.243 mmol), warmed to 55°, stirred for 2 h, diluted with $CHCl_3$ (4.0 ml), washed with sat. aq. $Na_2S_2O_3$ soln. (1.0 ml) and brine (0.7 ml), dried (Na_2SO_4), and evaporated. FC (0.75 g of silica gel; hexane/AcOEt 5 :4) gave **11** [1] (12.2 mg, 82%).

N^6-*Benzoyl-8-chloro-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-adenine* (**13**). At 25°, a soln. of **12** [1] (149.1 mg, 0.275 mmol) in dry THF (4.5 ml) was treated with 1.0M soln. of TBAF in THF (0.42 ml, 0.42 mmol), stirred for 7 h, and evaporated. FC (7 g of silica gel; $CHCl_3$/AcOEt 3 :2) gave the desilylated propargyl alcohol (119.0 mg, 92%). At 25°, a soln. of this alcohol (548.0 mg, 1.17 mmol) and imidazole (246.0 mg, 3.61 mmol) in dry DMF (16 ml) was treated dropwise with Et_3SiCl (0.59 ml, 3.51 mmol), stirred for 15 h, poured into ice-water (*ca.* 60 ml), and extracted with hexane/AcOEt 1 :1 (3 × 15 ml). The combined org. layers were washed with H_2O, dried (Na_2SO_4), and evaporated. FC (25 g of silica gel; hexane/AcOEt 5 :4) gave **13** (466.4 mg, 73%). White solid. R_f (hexane/AcOEt 5 :4) 0.50. M.p. 73°. $[\alpha]_D^{25} = -19.6$ (*c* = 1.02, $CHCl_3$). UV ($CHCl_3$): 279 (19000), 240 (18500). IR ($CHCl_3$): 3408*w* (br.), 3306*w*, 3007*w*, 2958*w*, 2914*w*, 2878*w*, 2100*w*, 1711*m*, 1611*s*, 1589*m*, 1508*w*, 1480*w*, 1450*s*, 1416*w*, 1384*w*, 1376*w*, 1357*w*, 1323*m*, 1248*m*, 1159*w*, 1093*s*, 1005*w*, 973*w*, 892*w*, 872*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 0.62 (*q*, *J* = 8.2), 0.63 (*q*, *J* = 8.0) ((MeC*H*$_2$)$_3$Si); 0.95 (*t*, *J* = 8.1, (*Me*CH$_2$)$_3$Si); 1.41, 1.62 (2*s*, Me$_2$C); 7.48–7.56 (*m*, 2 arom. H); 7.58–7.65 (*m*, 1 arom. H); 7.97–8.03 (*m*, 2 arom. H); 8.98 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4 (*s*, C=O); 152.5 (*d*, C(2)); 151.7 (*s*, C(6)); 148.5 (*s*, C(4)); 141.9 (*s*, C(8)); 133.4 (*s*); 133.0 (*d*); 128.9 (2*d*); 127.8 (2*d*); 121.7 (*s*, C(5)); 114.4 (*s*, Me$_2$*C*); 90.9 (*d*, C(1′)); 89.9 (*d*, C(4′)); 82.6 (*d*, C(2′)); 82.2 (*s*, C(6′)); 82.0 (*d*, C(3′)); 74.1 (*s*, C(7′)); 62.5 (*d*, C(5′)); 27.2, 25.4 (2*q*, *Me*$_2$*C*); 6.6 (*q*, (*Me*CH$_2$)$_3$Si); 4.7 (*t*, (MeCH$_2$)$_3$Si). FAB-MS: 584 (100, [*M* + 1]$^+$), 585 (37), 586 (43), 587 (12). Anal. calc. for $C_{28}H_{34}ClN_5O_5Si$ (584.15): C 57.57, H 5.87, N 11.99; found: C 57.48, H 5.86, N 11.90.

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-8-{[(4-methoxyphenyl)methyl]amino}adenine* (**14**). At 25°, a soln. of **13** (597.5 mg, 1.02 mmol) in dry EtOH (18 ml) was treated with 4-methoxybenzylamine (0.40 ml, 3.06 mmol), stirred for 25 h, and evaporated. The residue was dissolved in $CHCl_3$ (60 ml), washed with sat. aq. $NaHCO_3$ soln. (20 ml) and brine (20 ml), dried (Na_2SO_4), and evaporated. FC (25 g of silica gel; hexane/AcOEt 1 :2) gave **14** (668 mg, 95%). White solid. R_f (hexane/AcOEt 1 :2) 0.42. M.p. 84°. [α] = −42.3 (*c* = 1.04, $CHCl_3$). UV ($CHCl_3$): 309 (19000), 245 (18000). IR ($CHCl_3$): 3400*w* (br.), 3305*w*, 3000*m*, 2959*m*, 2913*w*, 2878*w*, 2838*w*, 2100*w*, 1701*m*, 1620*s*, 1577*s*, 1514*s*, 1478*m*, 1452*s*, 1424*m*, 1384*m*, 1329*m*, 1303*m*, 1252*s*, 1174*m*, 1090*s*, 1036*w*, 1004*w*, 868*w*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 0.57 (*q*, *J* = 8.2), 0.58 (*q*, *J* = 8.0) ((MeC*H*$_2$)$_3$Si); 0.90 (*t*, *J* = 8.1, (*Me*CH$_2$)$_3$Si); 1.40, 1.60 (2*s*, Me$_2$C);

3.79 (*s*, MeO); 4.61 (*dd*, *J* = 15.0, 5.0), 4.67 (*dd*, *J* = 15.0, 5.0) (ArC*H*$_2$); 5.76–5.81 (br. *s*, HN–C(8)); 6.88, 7.31 (2*d*, *J* = 8.8, 4 arom. H); 7.46–7.56 (*m*, 2 arom. H); 7.56–7.62 (*m*, 1 arom. H); 7.98–8.04 (*m*, 2 arom. H); 8.91 (br. *s*, HN–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.7 (*s*, C=O); 159.2 (*s*); 153.5 (*s*, C(6)); 152.3 (*s*, C(4)); 149.2 (*d*, C(2)); 144.7 (*s*, C(8)); 134.4 (*s*); 132.3 (*d*); 129.8 (*s*); 129.2 (2*d*); 128.7 (2*d*); 127.8 (2*d*); 122.0 (*s*, C(5)); 114.8 (*s*, Me$_2$*C*); 114.1 (2*d*); 89.6 (*d*, C(1′)); 88.3 (*d*, C(4′)); 81.4 (*d,* C(2′)); 81.3 (*s*, C(6′)); 81.0 (*d,* C(3′)); 74.9 (*s*, C(7′)); 62.6 (*d*, C(5′)); 55.3 (*q*, MeO); 46.6 (*t*, ArC*H*$_2$); 27.1, 25.4 (2*q*, *Me*$_2$C); 6.6 (*q*, (*Me*CH$_2$)$_3$Si); 4.6 (*t*, (MeCH$_2$)$_3$Si). FAB-MS: 685 ([*M* + 1]$^+$).

Oxidation of **14** *with DDQ*. *a*) At 25°, a soln. of **14** (348 mg, 0.51 mmol) in dry CH_2Cl_2 (10.4 ml) was treated with DDQ (177.5 mg, 0.78 mmol), stirred for 4 h, diluted with $CHCl_3$ (20 ml), washed with sat. aq. $NaHCO_3$ soln. (15 ml) and brine (10 ml), dried (Na_2SO_4), and evaporated. FC (18 g of silica gel; hexane/AcOEt 1:2) gave **15** (301.4 mg, 87%).

b) Similarly, a mixture of **14** (314.9 mg, 0.460 mmol) and DDQ (152.4 mg, 0.671 mmol) in CH_2Cl_2/H_2O 18:1 (12.0 ml) was stirred for 4 h. Analogous workup gave **15** (56.2 mg, 18%) and **16** (160.0 mg, 62%).

Data of N^6*-Benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-β-*D*-*allo*-hept-6-ynofuranosyl]-8-[[(4-methoxyphenyl)methylidene]amino]adenine* (**15**): Yellow solid. R_f (hexane/AcOEt 3:4) 0.52. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 0.66 (*q*, *J* = 8.2), 0.67 (*q*, *J* = 8.0) ((MeC*H*$_2$)$_3$Si); 0.98 (*t*, *J* = 8.1, (*Me*CH$_2$)$_3$Si); 1.43, 1.66 (2*s*, Me$_2$C); 3.92 (*s*, MeO); 7.03, 8.03 (2*d*, *J* = 9.0, 4 arom. H); 7.51–7.59 (*m*, 2 arom. H); 7.59–7.66 (*m*, 1 arom. H); 7.98–8.04 (*m*, 2 arom. H); 8.93 (br. *s*, NH, exchange with D_2O); 9.39 (*s*, CH=N).

*Data of 8-Amino-*N^6*-benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-β-*D*-*allo*-hept-6-ynofuranosyl]adenine* (**16**): Light orange solid. R_f ($CHCl_3$/AcOEt 1:2) 0.50. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 0.73 (*q*, *J* = 8.2), 0.74 (*q*, *J* = 8.0) ((MeC*H*$_2$)$_3$Si); 0.99 (*t*, *J* = 8.1, (*Me*CH$_2$)$_3$Si); 1.42, 1.67 (2*s*, Me$_2$C); 5.64 (br. *s*, NH$_2$); 7.44–7.63 (*m*, 3 arom. H); 7.96–8.04 (*m*, 2 arom. H); 8.76 (br. *s*, NH).

N^6*-Benzoyl-2′,3′-*O*-isopropylidene-5′-*O*-(triethylsilyl)adenosin-8-yl-(8 → 7′)-8-amino-*N^6*-benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-β-*D*-allo-hept-6-ynofuranosyl]adenine* (**17**). At 25°, a soln. of **5** (287.6 mg, 0.44 mmol) and **15** (301.4 mg, 0.38 mmol) in dry Et_3N (18 ml) was treated with CuI (8.2 mg, 43 μmol), P(fur)3 (5.4 mg, 25.8 μmol) and [Pd_2(dba)$_3$] (12.0 mg, 13 μmol), stirred for 3 h, warmed to 80°, stirred for 2 h, and evaporated. The residue was dissolved in $CHCl_3$ (60 ml) and washed with 2% aq. Na_2(EDTA) soln. (2 × 15 ml). Drying (Na_2SO_4), evaporation, and FC (25 g of silica gel; hexane/acetone 5:4) gave **17** (336.3 mg, 70%). Yellow solid. R_f (hexane/acetone 5:4) 0.46. M.p. 144°. $[\alpha]_D^{25} = +91.2$ (*c* = 1.02, $CHCl_3$). UV ($CHCl_3$): 304 (47000), 248 (32000). IR ($CHCl_3$): 3450*w* (br.), 3402*w* (br.), 3338*w* (br.), 3001*m*, 2959*m*, 2913*w*, 2878*w*, 1706*m*, 1637*s*, 1609*s*, 1584*s*, 1501*m*, 1478*s*, 1436*m*, 1385*m*, 1331*m*, 1254*s*, 1170*m*, 1158*m*, 1090*s*, 1003*w*, 972*w*, 866*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.50 (*q*, *J* = 8.0, (MeC*H*$_2$)$_3$Si); 0.710 (*q*, *J* = 8.0), 0.715 (*q*, *J* = 7.8) ((MeC*H*$_2$)$_3$Si); 0.87, 0.99 (2*t*, *J* = 8.0, 2 (*Me*CH$_2$)$_3$Si); 1.40, 1.42, 1.62, 1.64 (4*s*, 2 Me$_2$C); 6.06–6.36 (br. *s*, NH$_2$); 7.47, 7.52 (2*t*, *J* = 8.0, 4 arom. H); 7.53–7.61 (*m*, 2 arom. H); 7.98 (*d*, *J* = 8.0, 4 arom. H); 9.27 (br. *s*, 2 NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.0 (*s*, 2 C=O); 153.6, 152.2 (2*s*, C(6/I), C(6/II)); 153.3, 149.2 (2*d*, C(2/I), C(2/II)); 150.6, 149.8 (2*s*, C(4/I), C(4/II)); 144.6 (*s*, C(8/I)); 136.2 (*s*, C(8/II)); 133.8, 133.4 (2*s*); 132.8, 132.3 (2*d*); 128.7 (2*d*); 128.6 (2*d*); 128.0 (2*d*); 127.8 (2*d*); 123.0, 122.1 (2*s*, C(5/I), C(5/II)); 115.0, 114.2 (2*s*, 2 Me$_2$*C*); 95.3 (*s*, C(6′/I)); 90.6, 89.2 (2*d*, C(1′/I), C(1′/II)); 88.5, 88.1 (2*d*, C(4′/I), C(4′/II)); 83.3, 82.1 (2*d*, C(2′/I), C(2′/II)); 82.0, 80.8 (2*d*, C(3′/I), C(3′/II)); 74.5 (*s*, C(7′/I)); 63.1 (*d*, C(5/I)); 63.0 (*t*, C(5/II)); 27.1, 27.0, 25.4, 25.3 (4*q*, 2 *Me*$_2$C); 6.6, 6.5 (2*q*, 2 (*Me*CH$_2$)$_3$Si); 4.6, 4.2 (2*t*, 2 (MeCH$_2$)$_3$Si). FAB-MS: 1088 ([*M* + 1]$^+$). Anal. calc. for $C_{54}H_{69}N_{11}O_{10}Si_2$ (1088.38): C 59.36, H 6.31, N 14.11; found: C 59.59, H 6.39, N 14.16.

N^6*-Benzoyl-2′,3′-*O*-isopropylidene-5′-*O*-(triethylsilyl)adenosin-8-yl-(8 → 7′)-*N^6*-benzoyl-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-β-*D*-allo-hept-6-ynofuranosyl]-8-iodoadenine* (**18**). At 25°, a suspension of **17** (123.7 mg, 0.114 mmol) in CH_2I_2 (1.9 ml) was treated with $C_5H_{11}ONO$ (0.31 ml, 2.3 mmol), KI (64.2 mg, 0.39 mmol) and I_2 (102.2 mg, 0.4 mmol), warmed to 55°, stirred for 20 min, diluted with $CHCl_3$ (15 ml), washed with sat. aq. $Na_2S_2O_3$ soln. (3 ml) and brine (3 ml), dried (Na_2SO_4), and evaporated. FC (18 g of silica gel; hexane/AcOEt 3:5) gave **18** (75.1 mg, 55%). Yellow solid. R_f (hexane/AcOEt 3:5) 0.48. M.p. 119°. $[\alpha]_D^{25} = +17.6$ (*c* = 0.57, $CHCl_3$). UV ($CHCl_3$): 293 (41000), 263 (22000). IR (KBr): 3450*w* (br.), 3410*w* (br.), 3220*w* (br.), 3062*w*, 2954*m*, 2912*w*, 2877*m*, 1706*m*, 1606*s*, 1583*s*, 1509*m*, 1459*m*, 1425*m*, 1382*w*, 1326*m*, 1245*s*, 1214*m*, 1158*m*, 1093*s*, 1004*w*, 974*w*, 870*w*, 798*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.50 (*q*, *J* = 8.0, (MeC*H*$_2$)$_3$Si); 0.710 (*q*, *J* = 8.0), 0.715 (*q*, *J* = 7.8) ((MeC*H*$_2$)$_3$Si); 0.87, 1.01 (2*t*, *J* = 8.0, 2 (*Me*CH$_2$)$_3$Si); 1.38, 1.43, 1.61, 1.66 (4*s*, 2 Me$_2$C); 7.47–7.65 (*m*, 6 arom. H); 7.94–8.02 (*m*, 4 arom. H); 8.95, 9.01 (2 br. *s*, 2 NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.4, 164.3 (2*s*, 2 C=O); 153.4, 152.4 (2*d*, C(2/I), C(2/II)); 151.6, 150.2 (2*s*, C(6/I), C(6/II)); 149.5, 148.4 (2*s*, C(4/I), C(4/II)); 136.6 (*s*, C(8/II)); 133.7, 133.5 (2*s*); 133.0, 132.8 (2*d*); 128.9 (4*d*); 127.8 (4*d*); 125.6 (*s*, C(5/I)); 122.5 (*s*, C(5/II)); 114.5, 114.1 (2*s*, 2 Me$_2$*C*); 104.8 (*s*, C(8/I)); 96.9 (*s*, C(6′/I)); 93.9, 90.7 (2*d*, C(1′/I), C(1′/II)); 89.8, 88.1 (2*d*, C(4′/I), C(4′/II)); 83.2, 83.1 (2*d*, C(2′/I), C(2′/II)); 82.4, 82.2 (2*d*, C(3′/I), C(3′/

Table 4. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Dimers* **17**, **18**, **22**, *and* **23**, *and the Tetramers* **24**–**26** *in $CDCl_3$ Solution*

	17		**18**		**22**		**23**[a])	
	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I
H–C(2)	8.79	8.56	8.79	8.73	8.34[b])	8.26[b])	8.34[b])	8.28[b])
H–C(8)	–	–	–	–	8.18	–	8.15	–
H–C(1′)	6.33	6.26	6.26[b])	6.20[b])	6.21	6.45	6.23	6.33
H–C(2′)	5.70	5.65	5.72	5.63	5.64	5.60	5.61	5.55
H–C(3′)	5.15	5.19	5.13	5.40	5.24	5.26	5.245	5.22
H–C(4′)	4.31	4.36	4.28	4.44	4.17	4.51	4.21	4.50
H_a–C(5′)	3.66	4.83	3.66	4.89	4.55	4.81	4.64	4.84
H_ab–C(5′)[d])	3.79	–	3.78	–	–	–	2.33	–
J(1′,2′)	1.8	2.0	2.0	2.0	1.8	< 1.0	2.0	2.0
J(2′,3′)	6.5	6.5	6.5	6.5	6.5	6.5	6.4	6.3
J(3′,4′)	3.5	3.5	3.5	3.5	3.0	2.5	3.0	2.5
J(4′,5′a)	6.5	5.5	6.5	8.0	8.5	7.5	8.2	7.0
J(4′,5′b)	7.0	–	6.5	–	–	–	–	–
J(5′a,5′b)[e])	10.8	–	10.8	–	–	–	2.1	–

	24				**25**[f])				**26**[f])			
	Unit IV	Unit III	Unit II	Unit I	Unit IV	Unit III	Unit II	Unit I	Unit IV	Unit III	Unit II	Unit I
H–C(2)	8.76[b])	8.79[b])	7.99[c])	8.01[c])	8.65[b])	8.69[b])	8.09[c])	8.10[c])	8.16[b])	8.15[b])	8.15[b])	8.14[b])
H–C(8)	–	–	–	8.24	–	–	–	8.25	–	–	–	8.32
H–C(1′)	6.22[b])	6.13[b])	6.17[b])	6.45	6.18[b])	6.15[b])	6.11[b])	6.04	6.23[b])	6.18[b])	6.15[b])	6.04
H–C(2′)	5.64	5.55[b])	5.575[b])	5.59[b])	5.47[b])	5.36[b])	5.45[b])	5.29[b])	5.44[b])	5.42[b])	5.42[b])	5.38[b])
H–C(3′)	5.14	5.37	5.13	5.41	4.92	5.17[b])	5.21[b])	5.11	4.95	5.21[b])	5.23[b])	5.18
H–C(4′)	4.24	4.41	4.40	4.35	4.01	4.18[b])	4.20[b])	4.24	4.12	4.23[b])	4.26[b])	4.30
H_a–C(5′)	3.63	4.89	4.97	4.98	[g])	4.87[b])	4.88[b])	4.78	3.46	4.91	4.91	4.85
H_b–C(5′)	3.75	–	–	–	[g])	–	–	–	3.55	–	–	–
J(1′,2′)	2.0	1.5[b])	2.0[b])	1.5	2.5[b])	3.0[b])	3.0[b])	3.0	3.0	3.0	3.0	3.0
J(2′,3′)	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
J(3′,4′)	3.5	4.0	2.5	3.5	3.5	3.0	3.0	2.5	3.0	3.0[b])	2.5[b])	2.5
J(4′,5′a)	6.5	8.0	8.8	7.5	5.5	7.5[b])	8.0[b])	6.5	5.0	6.5[b])	6.0[b])	6.5
J(4′,5′b)	6.5	–	–	–	5.5	–	–	–	5.0	–	–	–
J(5′a,5′b)	10.8	–	–	–	[h])	–	–	–	12.0	–	–	–

[a]) Assignment based on a DQFCOSY.GRASP spectrum. [b]) [c]) Assignment to the units may be interchanged. [d]) H–C(7′) of **23**. [e]) J(5′,7′) of **23**. [f]) In (D_6)DMSO. [g]) At 3.35–3.5 ppm, partially hidden by the HDO signal. [h]) Not determined.

II)); 73.7 (*s*, C(7′/I)); 63.3 (*d*, C(5′/I)); 63.0 (*t*, C(5′/II)); 27.2, 25.4 (2*q*, 2 *Me*$_2$C); 6.7, 6.6 (2*q*, 2 (*Me*CH$_2$)$_3$Si); 4.7, 4.2 (2*t*, 2 (MeCH$_2$)$_3$Si). FAB-MS: 1199 ([$M+1$]$^+$). Anal. calc. for $C_{54}H_{67}IN_{10}O_{10}Si_2$ (1199.26): C 54.08, H 5.63, N 11.68; found: C 54.09, H 5.70, N 11.62.

9-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-5*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-8-iodoadenine* (**20**). At 25°, a soln. of **19** [1] (156.5 mg, 0.21 mmol) in dry toluene (4.7 ml) was treated with 4-methoxybenzylamine (0.14 ml, 1.07 mmol), stirred at 80° for 3 h, and evaporated. FC (10 g of silica gel; $CHCl_3$/AcOEt 4:5) gave **20** (114.5 mg, 81%). White solid. R_f ($CHCl_3$/AcOEt 1:1) 0.56. M.p. 79°. $[\alpha]_D^{25} = -12.3$ (c = 1.04, $CHCl_3$). UV ($CHCl_3$): 266 (15000). IR ($CHCl_3$): 3400*w* (br.), 2959*m*, 2913*w*, 2877*m*, 2173*w*, 1631*s*, 1584*m*, 1520*w*, 1476*m*, 1442*m*, 1417*m*, 1384*m*, 1358*m*, 1321*m*, 1287*m*, 1248*s*, 1158*m*, 1091*s*, 1049*m*, 1004*m*, 929*m*, 846*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 0.09 (*s*, Me_3Si); 0.61 (*q*, J = 9.1), 0.62 (*q*, J = 9.1) ((MeC*H*$_2$)$_3$Si); 0.94 (*t*, J = 8.1, (*Me*CH$_2$)$_3$Si); 1.40, 1.61 (2*s*, Me_2C); 5.95 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.0 (*s*, C(6)); 152.4 (*d*, C(2)); 150.4 (*s*, C(4)); 122.7 (*s*, C(5)); 113.8 (*s*, Me_2C); 104.1 (*s*, C(8)); 101.0 (*s*, C(6′)); 93.9 (*d*, C(1′)); 90.6 (*s*, C(7′)); 90.0 (*d*, C(4′)); 82.9 (*d*, C(2′)); 82.5 (*d*, C(3′)); 63.0 (*d*, C(5′)); 27.1, 25.4 (2*q*,

Me$_2$C); 6.7 (*q*, (*Me*CH$_2$)$_3$Si); 4.8 (*t*, (MeCH$_2$)$_3$Si); −0.3 (*q*, Me$_3$Si). FAB-MS: 644 ([*M* + 1]$^+$). Anal. calc. for $C_{24}H_{38}IN_5O_4Si_2$ (643.67): C 44.78, H 5.95, N 10.88; found: C 44.95, H 6.11, N 10.79.

9-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-7*-C-*(trimethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-adenin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**22**). At 25°, a soln. of **20** (268.2 mg, 0.4 mmol) and **21** [2] (178.2 mg, 0.4 mmol) in dry Et$_3$N (13.4 ml) was treated with CuI (8.3 mg, 43.6 μmol), P(fur)$_3$ (6.5 mg, 28 μmol) and [Pd$_2$(dba)$_3$] (12.3 mg, 13.4 μmol), stirred for 3 h, and evaporated. The residue was dissolved in CHCl$_3$ (60 ml) and washed with 2% aq. Na$_2$(EDTA) soln. (2 × 15 ml). Drying (Na$_2$SO$_4$), evaporation, and FC (20 g of silica gel; CHCl$_3$/acetone 1:2) gave **22** (326.9 mg, 85%). Light yellow solid. R_f (CHCl$_3$/acetone 1:2) 0.56. M.p. 128°. $[\alpha]_D^{25} = +19.8$ ($c = 1.00$, CHCl$_3$). UV (CHCl$_3$): 296 (21000), 266 (21000). IR (CHCl$_3$): 3412*w*, 3380*w*, 3208*w*, 2992*w*, 2958*m*, 2913*w*, 2878*w*, 2173*w*, 1701*w*, 1633*s*, 1588*m*, 1472*w*, 1414*w*, 1375*m*, 1328*m*, 1296*m*, 1248*w*, 1157*w*, 1095*s*, 1004*m*, 856*w*, 846*m*. ^{1}H-NMR (300 MHz, CDCl$_3$): see *Table 4*; additionally, 0.07 (*s*, Me$_3$Si); 0.60–0.77 (*m*, 2 (MeC*H*$_2$)$_3$Si); 0.97, 0.99 (2*t*, *J* = 8.0, 2 (*Me*CH$_2$)$_3$Si); 1.36, 1.44, 1.57, 1.65 (4*s*, 2 Me$_2$C); 6.43 (br. *s*, NH$_2$); 6.9–7.3 (br. *s*, NH$_2$). ^{13}C-NMR (75 MHz, CDCl$_3$): 155.8 (*s*, C(6/I), C(6/II)); 153.8, 152.9 (2*d*, C(2/I), C(2/II)); 149.0, 148.6 (2*s*, C(4/I), C(4/II)); 140.7 (*d*, C(8/I)); 133.8 (*s*, C(8/II)); 120.1, 119.4 (2*s*, C(5/I), C(5/II)); 114.2, 113.7 (2*s*, 2 Me$_2$*C*); 104.8 (*s*, C(6′/II)); 94.9 (*s*, C(6′/I)); 91.5, 90.8 (2*d*, C(1′/I), C(1′/II)); 90.3 (*s*, C(7′/II)); 90.2, 89.9 (2*d*, C(4′/I), C(4′/II)); 84.0, 83.3 (2*d*, C(2′/I), C(2′/II)); 82.9, 82.6 (2*d*, C(3′/I), C(3′/II)); 74.5 (*s*, C(7′/I)); 63.5, 63.3 (2*d*, C(5′/I), C(5′/II)); 27.1, 27.0, 25.5, 25.4 (4*q*, 2 *Me*$_2$C); 6.8, 6.7 (2*q*, 2 (*Me*CH$_2$)$_3$Si); 4.8, 4.7 (2*t*, 2 (MeCH$_2$)$_3$Si); −0.3 (*q*, Me$_3$Si). FAB-MS: 961 ([*M* + 1]$^+$).

9-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-yno-furanosyl]adenin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**23**). At 25°, a soln. of **22** (55.8 mg, 58 μmol) in THF (0.84 ml) was treated with a soln. of AgNO$_3$ (25.4 mg, 0.15 mmol) in 75% aq. MeOH (0.84 ml), stirred for 4.5 h, diluted with CHCl$_3$ (12 ml), washed with 5% aq. KCN soln. (5 ml) and brine (3 ml), dried (Na$_2$SO$_4$), and evaporated. At 25°, a soln. of the residue and imidazole (25.4 mg, 0.37 mmol) in dry DMF (1.7 ml) was treated dropwise with Et$_3$SiCl (49 μl, 0.29 mmol), stirred for 48 h, and poured into ice-water (*ca.* 3.5 ml). After extraction with Et$_2$O/AcOEt 1:1 (3 × 1.2 ml), the combined org. layers were washed with H$_2$O, dried (Na$_2$SO$_4$), and evaporated. FC (3.0 g of silica gel; CHCl$_3$/acetone 2:3) gave **23** (37.0 mg, 72%). Light yellow solid. R_f (CHCl$_3$/acetone 2:3) 0.46. M.p. 126°. $[\alpha]_D^{25} = +33.8$ ($c = 1.02$, CHCl$_3$). UV (CHCl$_3$): 296 (20000), 266 (21000). IR (CHCl$_3$): 3411*w*, 3307*w*, 3207*w*, 3008*s*, 2975*m*, 2914*m*, 2878*m*, 1633*s*, 1588*m*, 1520*w*, 1474*m*, 1421*m*, 1384*m*, 1375*m*, 1329*m*, 1296*m*, 1248*s*, 1157*m*, 1097*s*, 1048*s*, 1006*m*, 971*w*, 928*m*, 873*m*, 850*m*, 818*m*. ^{1}H-NMR (500 MHz, CDCl$_3$, assignment based on a DQFCOSY.GRASP spectrum): see *Table 4*; additionally, 0.61–0.78 (*m*, 2 (MeC*H*$_2$)$_3$Si); 0.98 (*t*, *J* = 7.8, 2 (*Me*CH$_2$)$_3$Si); 1.38, 1.44, 1.59, 1.65 (4*s*, 2 Me$_2$C); 6.23, 6.70 (2 br. *s*, 2 NH$_2$). ^{13}C-NMR (75 MHz, CDCl$_3$): 155.9 (*s*, C(6/I), C(6/II)); 153.8, 152.9 (2*d*, C(2/I), C(2/II)); 148.9, 148.6 (2*s*, C(4/I), C(4/II)); 140.6 (*d*, C(8/I)); 133.7 (*s*, C(8/II)); 120.1, 119.5 (2*s*, C(5/I), C(5/II)); 114.2, 113.8 (2*s*, 2 Me$_2$*C*); 95.1 (*s*, C(6′/I)); 91.5, 90.9 (2*d*, C(1′/I), C(1′/II)); 90.2, 90.0 (2*d*, C(4′/I), C(4′/II)); 84.0, 83.4 (2*d*, C(2′/I), C(2′/II)); 83.0, 82.7 (2*d*, C(3′/I), C(3′/II)); 74.3 (*s*, C(7′/I)); 73.6, 73.5 (2*s*, C(6′/II), C(7′/II)); 63.5, 62.6 (2*d*, C(5′/I), C(5′/II)); 27.1, 27.0, 25.4, 25.3 (4*q*, 2 *Me*$_2$C); 6.7 (*q*, 2 (*Me*CH$_2$)$_3$Si); 4.7 (*t*, 2 (MeCH$_2$)$_3$Si). FAB-MS: 889 ([*M* + 1]$^+$). Anal. calc. for $C_{42}H_{60}N_{10}O_8Si_2$ (889.17): C 56.56, H 6.79, N 15.66; found: C 56.73, H 6.80, N 15.75.

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosin-8-yl-(8 → 7′)*-N^6-*benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**24**). At 25°, a soln. of **18** (81.5 mg, 68 μmol) and **23** (60.5 mg, 68 μmol) in dry Et$_3$N/toluene 1:1 (4.2 ml) was treated with CuI (1.7 mg, 8.9 μmol), P(fur)$_3$ (1.2 mg, 5.2 μmol) and [Pd$_2$(dba)$_3$] (2.2 mg, 2.4 μmol), stirred for 11 h, and evaporated. The residue was dissolved in CHCl$_3$ (16 ml) and washed with 2% aq. Na$_2$EDTA soln. (2 × 4 ml). Drying (Na$_2$SO$_4$), evaporation, and FC (7.0 g of silica gel; CHCl$_3$/acetone 1:1) gave **24** (105.2 mg, 79%). Light yellow solid. R_f (CHCl$_3$/acetone 1:1) 0.50. M.p. 152°. $[\alpha]_D^{25} = -6.9$ ($c = 1.06$, CHCl$_3$). UV (CHCl$_3$): 316 (sh. 61000), 304 (71000), 296 (71000), 251 (55000). IR (CHCl$_3$): 3411*w* (br.), 3370*w*, 2976*s*, 2894*m*, 1709*w*, 1633*m*, 1608*m*, 1585*m*, 1519*s*, 1475*s*, 1423*s*, 1386*m*, 1330*m*, 1080*s*, 1047*s*, 929*s*, 876*s*, 850*s*. ^{1}H-NMR (300 MHz, CDCl$_3$): see *Table 4*; additionally, 0.48 (*q*, *J* = 8.0, (MeC*H*$_2$)$_3$Si); 0.55–0.77 (*m*, 3 (MeC*H*$_2$)$_3$Si); 0.85, 0.89, 0.95, 0.98 (4*t*, *J* = 8.0, 4 (*Me*CH$_2$)$_3$Si); 1.37, 1.39 (2 Me); 1.40, 1.56, 1.58, 1.61, 1.68 (7*s*, 4 Me$_2$C); 6.27 (br. *s*, NH$_2$); 6.65 (br. *s*, NH$_2$); 7.36 (*t*, *J* = 7.8, 2 arom. H); 7.41–7.58 (*m*, 4 arom. H); 7.90, 7.94 (2*d*, *J* = 7.8, 4 arom. H); 9.24, 9.83 (2 br. *s*, 2 NH). ^{13}C-NMR (75 MHz, CDCl$_3$): 164.9, 164.6 (2*s*, 2 C=O); 156.2, 155.7 (2*s*, C(6/I), C(6/II)); 153.7, 153.5, 153.3, 152.9 (4*d*, C(2/I–IV)); 150.2, 150.1 (2*s*, C(6/III), C(6/IV)); 149.7, 148.6 (2*s*, C(4/I–IV)); 140.7 (*d*, C(8/I)); 136.8, 136.6, 133.9 (3*s*, C(8/II–IV)); 133.6 (2*s*); 132.7 (2*d*); 128.8 (2*d*); 128.7 (2*d*); 128.0 (2*d*); 127.9 (2*d*); 122.6, 122.5 (2*s*, C(5/III–IV)); 120.3, 119.6 (2*s*,

C(5/I–II)); 114.3 (2 C), 114.1, 114.0 (3*s*, 4 Me_2C); 97.7, 97.2, 95.3 (3*s*, C(6′/I–III)); 92.1, 90.7, 90.6, 90.1 (4*d*, C(1′/I–IV)); 89.9, 89.6, 89.3, 88.2 (4*d*, C(4′/I–IV)); 83.7, 83.5 (2 C), 83.3 (3*d*, C(2′/I–IV)); 82.9, 82.2 (2 C), 81.9 (3*d*, C(3′/I–IV)); 74.2, 73.5, 73.2 (3*s*, C(7′/I–III)); 63.3, 63.2, 63.1 (3*d*, C(5′/I–III)); 62.9 (*t*, C(5′/IV)); 27.2 (3 C), 26.9, 25.5, 25.4 (2 C), 25.3 (5*q*, 4 Me_2C); 6.8 (*q*, 3 ($MeCH_2$)$_3$Si); 6.6 (*q*, ($MeCH_2$)$_3$Si); 4.80, 4.75, 4.70, 4.2, (4*t*, 4 ($MeCH_2$)$_3$Si). FAB-MS: 1961 ($[M+1]^+$). Anal. calc. for $C_{96}H_{126}N_{20}O_{18}Si_4$ (1960.52): C 58.81, H 6.48, N 14.29; found: C 58.20, H 6.79, N 13.80.

N^6-*Benzoyl-2′,3′*-O-*isopropylideneadenosin-8-yl-(8 → 7′)*-N^6-*benzoyl-9-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)adenin-8-yl-(8 → 7′)-9-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)adenin-8-yl-(8 → 7′)-9-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)adenine* (**25**). At 25°, a soln. of **24** (90 mg, 45.9 μmol) in 50% aq. THF (1.8 ml) was treated with AcOH (1.8 ml), stirred for 21 h, evaporated, and co-evaporated several times with toluene. A soln. of the residue in toluene/MeOH 1:1 (1.0 ml) was treated with SiO_2 (242 mg), evaporated, and the residue was charged on a silica-gel column. FC (4.0 g of silica gel; $CHCl_3$/MeOH 8:1) gave crude **25** (61.3 mg, 89%). Yellow solid. R_f ($CHCl_3$/MeOH 8:1) 0.48. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 4*; additionally, 1.17, 1.24 (2 Me), 1.27, 1.37, 1.44, 1.45, 1.46 (7*s*, 4 Me_2C); 3.35–3.50 (*m*, partially hidden by HDO signal, addn. of D_2O → change, 2 H–C(5′/IV), 2 NH_2); 4.78 (br. *t*, $J \approx 6.0$, addn. of D_2O → *d*, $J = 6.5$, H–C(5′/I)); 4.85 (br. *t*, $J \rightarrow 6.5$, addn. of D_2O → 4.87, *d*, $J = 7.5$, → 4.88, *d*, $J = 8.0$, H–C(5′/II–III)); 4.88–4.96 (signal hidden by a H–C(3) signal, exchange with D_2O, HO–C(5′/IV)); 6.59 (br. *d*, $J \approx 6.0$, exchange with D_2O), 6.66 (br. *d*, $J \approx 5.5$, exchange with D_2O), 6.78 (br. *d*, $J \approx 5.0$, exchange with D_2O) (HO–C(5′/I–III)); 7.32 (br. *s*, exchange with D_2O, 2 NH); 7.44–7.53 (*m*, 4 arom. H); 7.56–7.63 (*m*, 2 arom. H); 7.91–7.99 (*m*, 4 arom. H).

2′,3′-O-*Isopropylideneadenosin-8-yl-[(8 → 7′)-9-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)adenin-8-yl]$_2$-(8 → 7′)-9-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)adenine* (**26**). At 25°, a soln. of **25** (72.7 mg, 48.4 μmol) in MeOH (0.73 ml) was treated with toluene (0.73 ml) and 25% aq. NH_4OH (1.5 ml), stirred for 3.5 h, evaporated, and co-evaporated several times with toluene. A soln. of the residue in toluene/MeOH 1:1 (2.0 ml) was treated with SiO_2 (316 mg), evaporated, and the residue was charged on a silica-gel column. FC (6.0 g of silica gel; $CHCl_3$/MeOH 5:1) gave crude **26** (15.4 mg, 25%). Light yellow solid. R_f ($CHCl_3$/MeOH 5:1) 0.53. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 4*; additionally, 1.26, 1.29, 1.31, 1.33, 1.45, 1.49, 1.52, 1.54 (8*s*, 4 Me_2C); 3.46 (*dt*, $J \approx 12.0$, 5.5, addn. of D_2O → *dd*, $J = 12.0$, 5.0, H_a–C(5′/IV)); 3.55 (*dt*, $J = 12.0$, 5.5, addn. of D_2O → *dd*, $J = 12.0$, 5.0, H_b–C(5′/IV)); 4.85 (br. *t*, $J \approx 6.0$, addn. of D_2O → 4.83, *d*, $J = 6.5$, H–C(5′/I)); 4.91 (br. *t*, $J \approx 6.5$, addn. of D_2O → 4.87, *d*, $J = 6.0$, → 4.895, *d*, $J = 6.5$, H–C(5′/II–III)); 5.24 (br. *t*, $J \approx 6.0$, exchange with D_2O, HO–C(5′/IV)); 6.71 (br. *d*, $J \approx 5.5$, exchange with D_2O), 6.74 (br. *d*, $J \approx 6.0$, exchange with D_2O), 6.76 (br. *d*, $J \approx 5.0$, exchange with D_2O) (HO–C(5′/I–III)); 7.37 (br. *s*, exchange with D_2O, NH_2); 7.50–7.80 (br. *s*, 3 NH_2).

Adenosin-8-yl-[(8 → 7′)-9-(6,7-dideoxy-β-D-allo-*hept-6-ynofuranosyl)adenin-8-yl]$_2$-(8 → 7′)-9-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)adenine* (**27**). At 25°, a soln. of crude **26** (30.6 mg) in 80% aq. HCO_2H (1.0 ml) was stirred for 22 h, evaporated, and co-evaporated several times with toluene. Recrystallisation from DMSO/MeOH gave **27** (13.9 mg, 72%). White plates. M.p. 187° (dec.). R_f (BuOH/EtOH/H_2O 1:1:1) 0.06. $[\alpha]_D^{25} = -94.2$ ($c = 0.45$, DMSO). UV (DMSO): 311 (sh, 29500), 301 (48000), 278 (28000). IR (KBr): 3600–2500*s* (br.), 1716*w*, 1651*s*, 1602*s*, 1575*m*, 1485*w*, 1423*w*, 1374*m*, 1331*s*, 1303*m*, 1255*m*, 1126*m*, 1075*m*, 1040*m*, 970*w*, 909*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO/D_2O): 3.6–3.8 (*m*, partially hidden by HDO signal, 2 H–C(5′/IV)); 3.94–4.01 (*m*, H–C(4′/IV)); 4.10–4.20 (*m*, 4 H); 4.30–4.42 (*m*, 4 H); 4.72 (*dd*, $J = 7.5$, 5.0, H–C(2′/I)); 4.89 (*d*, $J = 4,7$), 4.97 (*d*, $J = 5.0$) (2 H–C(5′)); 4.96–5.05 (*m*, 3 H); 5.91 (*d*, $J = 7.5$), 5.95 (*d*, $J = 7.5$), 5.97 (*d*, $J = 7.5$), 6.00 (*d*, $J = 7.5$) (H–C(1′/I–IV)); 8.12, 8.14 (2 H), 8.15 (3*s*, H–C(2/I–IV)); 8.33 (*s*, H–C(8/I)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.5 (*s*, C(6/I–IV)); 153.5, 152.6 (2*d*, C(2/I–IV)); 149.2, 148.1 (2*s*, C(4/I–IV)); 140.2 (*d*, C(8/I)); 133.3 (*s*, C(8/II–IV)); 119.5 (*s*, C(5/I–IV)); 95.1, 95.0, 94.9 (3*s*, C(6′/I–III)); 89.6 (br.), 88.5 (2*d*, C(1′/I–IV)); 87.8, 86.8 (2*d*, C(4′/I–IV)); 73.5, 73.1 (2 br. *d*, C(2′/I–IV)); 71.6, 70.6 (2*d*, C(3′/I–IV)); 71.2, 71.0 (2*s*, C(7′/I–III)); 62.6, 62.5 (2*d*, C(5′/I–III)); 62.2 (*t*, C(5′/IV)).

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