Oligonucleosides with a Nucleobase-Including Backbone

Part 3

Synthesis of Acetyleno-Linked Adenosine Dimers

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

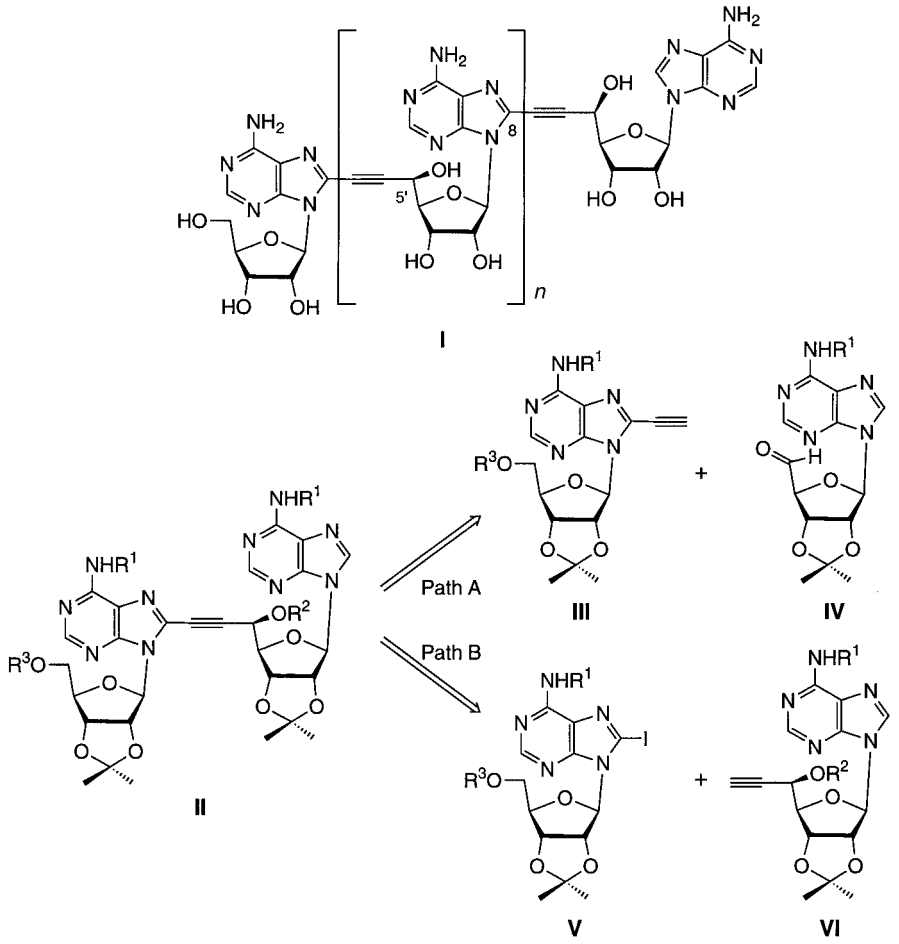
Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich

The adenosine-derived dimers **14a–d** and **15b–d** have been prepared by coupling the protected 8-iodoadenosines **3** and **13** with the C(5′)-ethynylated adenosine derivatives **5**, **6**, **11**, and **12** (*Scheme 4*). Similarly, the 5′-epimeric dimer **16** was prepared by coupling **3** with the alkyne **8** (*Scheme 5*). The propargylic alcohol **4** was transformed into the *N*-benzoylated alkyne **5** and into the amine **6**, while the epimeric alcohol **7** was converted to the epimeric amine **8** and the 5′-deoxy analogues **11** and **12** (*Scheme 3*). Cross-coupling of the iodoadenosine **13** with the alkyne **5** to **14a** was optimised; it is influenced by the *N*-benzoyl and the Et_3SiO group of the alkyne, but hardly by the *N*-benzoyl group of the 8-iodoadenosine. The alkyne is most reactive when it is *O*-silylated, but not *N*-benzoylated. Cross-coupling of the 5′-deoxyalkynes proceeded more slowly. The dimers **14a–d**, **15b–d**, and **16** were obtained in good yields (*Table 2*). Deprotection of **14d** and **16** led to **18** and **20**, respectively (*Scheme 5*). The diols **17** and **19** and the hexols **18** and **20** prefer the *syn*-conformation in (D_6)DMSO, completely for unit II and $\geq$80% for unit I; they exhibit partially persistent intramolecular O(5′)–H···N(3) H-bonds. The persistence increases from 18% (unit I of **19**), 32% (unit II of **17** and **19**), 45% (unit I of **17**), 52% (unit II of **18** and **20**), and 55% (unit I of **20**) to 82% (unit I of **18**).

Introduction. – We have designed oligonucleotide analogues in which the 3′,5′-phosphodiester moiety between adenosine units is replaced by an 8,5′-acetylene link (**I**, *Scheme 1*) [1]. Calculations predict that such adenosine-derived analogues may form stable complexes with uridine oligonucleotides and with their 6,5′-acetyleno-linked analogues. We have reported the synthesis of uridine- and adenosine-derived monomers [1][2] and of uridine-derived dimers [1], and we now describe the synthesis of protected and unprotected 8,5′-acetyleno-linked adenosine dimers **I** ($n = 0$; *Scheme 1*).

Formation of the 8,5′-ethynylidene link is the key to the synthesis of the projected oligonucleotide analogues. We have considered to construct the dimers **II** either by addition of acetylide anions derived from **III** to aldehydes **IV** (path *A*; *Scheme 1*), or by a *Sonogashira* reaction [3] of 8-iodoadenosines **V** and terminal heptynofuranosyl adenines **VI** (path *B*). In view of the low diastereoselectivity in the addition of [(trimethylsilyl)ethynyl]magnesium bromide to aldehydes of type **IV**, we have followed path *B* that takes advantage of working with monomers of established configuration [2]. Considering the sensitivity of the alkynylated adenosine derivatives to acid and base (as during deprotection), resulting in elimination of the propargylic OH group and degradation, we also planned to deoxygenate the alkynylated monomers and subject the products to cross-coupling with iodoadenosines of type **V**. In this context, we examined the dependence of the cross-coupling on the propargylic substituent at C(5′)

Scheme 1. *Acetyleno-Linked Adenosine Oligomers* **I** *and Retrosynthesis of the Dimer* **II**



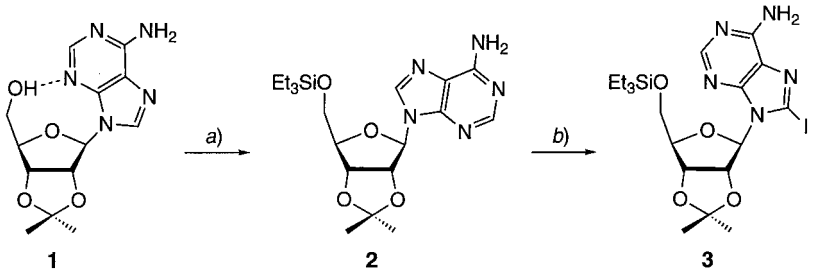
and also on the *N*-benzoyl group, preparing the eight dimers **14a**–**d**, **15b**–**d**, and **16** (the C(5′/I)[1]) epimer of **14d**) (*cf. Schemes 4* and *5*).

Results and Discussion. – We first prepared the required monomeric building block **3**. Triethylsilylation of the isopropylidenated adenosine **1** [4] afforded 70% of **2** (*Scheme 2*). Regioselective lithiation of **2** with LDA [5], followed by treatment with I_2 [2][6] yielded 87% of the 8-iodo derivative **3**.

The ^{1}H-NMR chemical shifts for the ribofuranosyl unit of the amine **2** (*cf. Table 4* in the *Exper. Part*) are similar to those of the corresponding N^6-benzoyl derivative [2] ($\Delta\delta = 0.06$ ppm for H–C(1′) and ≤ 0.03 for H–C(2′) to H–C(5′)) and evidence the

[1]) Starting from the downstream end, the units of the oligonucleosides are specified by roman numerals (*cf.* [1]).

Scheme 2



a) Et_3SiCl, imidazole, DMF; 70%. *b*) LDA, THF, then I_2; 87%.

anti-conformation. *N*-Debenzoylation leads to an upfield shift of 0.46 ppm for H–C(2) and of 0.2 ppm for H–C(8) of **2**[2]). The downfield shift of H–C(2′) of the iodide **3** (0.53 ppm relative to δ(H–C(2′)) of **2**) evidences a preferred *syn*-conformation, as it is typical for 8-substituted adenosines (*cf.* [2] and refs. cited there).

The other monomeric building blocks – the terminal acetylenes **5**, **6**, **8**, **11**, and **12** (*Scheme 3*) – were prepared from the epimeric propargylic alcohols **4** and **7** [2][8][3]). The building blocks derived from the (5′*R*)-configured monomer **4** serve as precursors for the dimers **14a–d**, and those derived from the (5′*S*)-configured monomer **7** as precursors for the dimer **16** and the deoxygenated dimers **15b–d** (*cf. Schemes 4* and *5*, and *Table 2*).

C-Desilylation and *O*-triethylsilylation of the propargylic alcohol **4** provided **5** in 86% yield. Hydrolysis of **4** and **7** with aqueous NH_4OH in MeOH [2], followed by treatment of the crude alcohols with Et_3SiCl in pyridine[4]) led to the epimeric *O*-silylated amines **6** and **8** in 91 and 67%, respectively (*Scheme 3*). The alcohol **7** was treated with (thiocarbonyl)diimidazole in CH_2Cl_2 to afford the thiocarbamate **9** (72%). Deoxygenation of **9** with Bu_3SnH/AIBN gave the 5′-deoxy derivative **10** (53% from **7**). Desilylation of **10** with TBAF in aqueous THF afforded the *N*-benzoylated [5′-deoxy-D-*ribo*-heptynofuranosyl]-adenine **11** quantitatively, while the corresponding debenzoylated derivative **12** was obtained in 97% yield by treating **10** with aqueous NH_4OH.

The ^{1}H-NMR chemical shifts and the vicinal couplings for the ribofuranosyl unit of **5**, **6**, and **8** (*Table 4* in the *Exper. Part*) are similar to those of the corresponding N^6-benzoylated and C(7′)-silylated analogues [2] ($\Delta\delta \leq 0.12$ ppm, $\Delta J \leq 0.5$ Hz). H–C(2′) of **5**, **6**, and **8** resonates at 5.25–5.27 ppm, evidencing the *anti*-conformation. H–C(2′) of the carbamate **9**, however, resonates at 5.53 ppm. The downfield shift of 0.27 ppm suggests a *ca.* 1:1 equilibrium between the *anti*- and the *syn*-conformers of **9**, as deduced from the downfield shift of *ca.* 0.55 ppm for H–C(2′) of corresponding L-*talo*-

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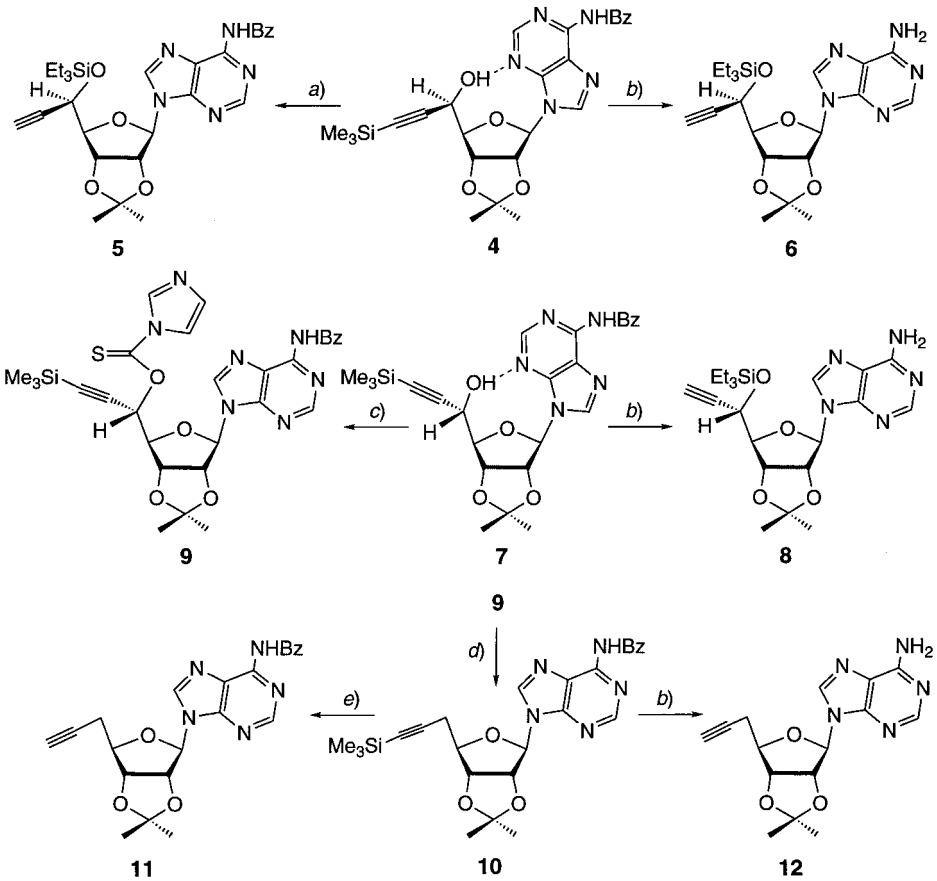
[2]) The assignment of H–C(2) and H–C(8) is based on the observation that the less deshielded *singlet* between 8.0 and 9.0 ppm disappears upon substitution of H–C(2) by a R–C≡C group (R=H or trialkylsilyl), while the more deshielded *singlet* is hardly influenced ($\Delta\delta < 0.1$ ppm) [7].

[3]) Independently of us, *Matsuda et al.* [8] have described the preparation of **4** and **7**; much to our regret, we noticed their results only after our communication [2] had been in print.

[4]) Pyridine was conveniently removed by co-evaporation with toluene (see *Exper. Part*), while the use of DMF instead of pyridine complicated the workup, as **4** and **7** were extracted together with traces of DMF that was not readily removed by chromatography.

Scheme 3



a) (TBAF) · 3 H_2O, THF; Et_3SiCl, imidazole, DMF; 86%. *b*) 25% aq. NH_4OH, MeOH; Et_3SiCl, pyridine; 91% (**6**), 67% (**8**), 97% (**12**). *c*) (Thiocarbonyl)diimidazole, CH_2Cl_2; 72%. *d*) Bu_3SnH, 2,2′-azobis[isobutyronitrile] (AIBN), toluene; 53% from **7**. *e*) TBAF · 3 H_2O, THF; 100%.

configured 8-haloadenosines [2], which adopt more or less completely the *syn*-conformation.

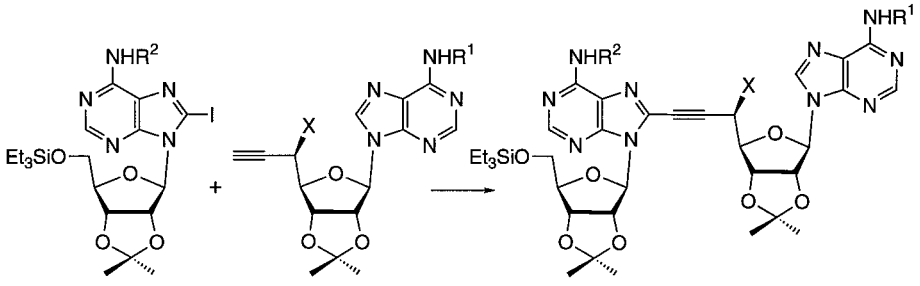
The *syn* ⇌ *anti* equilibrium influences the conformation of the propargylic side chain, as evidenced by $J(4',5')$ of 8.5 Hz for **9** and of 4.5–5.5 Hz for **5**, **6**, and **8**. The preferred conformer of **9** is characterized by an *antiperiplanar* arrangement of H–C(4′) and H–C(5′) bonds and exhibits the weakest steric interaction between the substituent at C(4) and the nucleobase. H–C(2′) of the D-*ribo*-heptynofuranosyl adenines **10**–**12** appears at 5.42–5.46 ppm, *ca.* 0.17 ppm downfield to H–C(2′) of **2** and *ca.* 0.36 ppm upfield to H–C(2′) of **3**, evidencing a *ca.* 2 : 1 equilibrium between the *anti*- and the *syn*-conformers of **10**–**12**. Again, the enhanced preference for the *syn*-conformer is paralleled by larger $J(4',5')$ couplings of 5.5–6.7 Hz for **10**–**12** *vs.* 4.0 Hz

for **2**. The $J(1',2')$ and $J(3',4')$ values evidence *ca.* 1:1 (*N*) $\rightleftharpoons$ (*S*)-equilibria for **2**, **3**, **5**, **6**, and **8**–**12**.

Due to the unusually large $^1J(^1H,^{13}C)$ and $^2J(^1H,^{13}C)$ couplings, the tertiary C-atom of terminal acetylenes does not lead to a signal in the DEPT spectrum, whereas the quaternary C-atom gives rise to a weak CH-type signal [9]. This has led to incorrect assignments of these signals (*cf.* [2][10] and earlier papers of this series)[5]). Monoalkylation of acetylene leads to a downfield shift of the signal for the C(α)-atom and to an upfield shift for the C(β)-atom [11]. Thus, the '*singlets*' of **5**, **6**, and **8** at 74.6–75.4 ppm are assigned to C(7′) and the '*doublets*' at 81.5–81.8 ppm to C(6′). Deoxygenation at C(5′) leads to upfield shifts of 2 ppm for C(6′) and of 4 ppm for C(7′) of **11** and **12**, whereas *C*-silylation leads to the expected downfield shift (*cf.* [10][12][13] and earlier papers of this series) for both C(6′) (**9**: 96.2, **10**: 101.5 ppm) and C(7′) (**9**: 91.2, **10**: 87.9 ppm).

To establish the best reaction conditions, we investigated the cross-coupling of **13** [2] and **5** (*Scheme 4* and *Table 1*). The conditions for the *Sonogashira* reaction [3] between 8-iodoadenosine and (trimethylsilyl)acetylene, providing 63% of the coupling product [14], led to a slow transformation; considerable amounts of starting material remaining after 3 h (*Table 1*, *Entry 1*). Prolonging the duration of the reaction (*Entry 2*) showed that the dimer **14a** is degraded under the reaction conditions. Optimisation of solvents and/or bases showed that DMF [15] is not suitable (*Entries 3* and *4*). Tertiary amines like Et_3N or *N*-methylpyrrolidine, used as solvents and bases, were superior to secondary amines [16], as they did not lead to *N*-debenzoylation (*Entries 1* and *6 vs. Entry 5*). However, no cross-coupling occurred in *Hünig*'s base or *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA; *Entries 7* and *8*). [$Pd_2(dba)_3$] in the presence of Et_3N or *N*-methylpyrrolidine proved the best catalyst (*Entries 9–17*). We

Scheme 4



13 R^2 = Bz
3 R^2 = H

5 R^1 = Bz, X = Et_3SiO
6 R^1 = H, X = Et_3SiO
11 R^1 = Bz, X = H
12 R^1 = H, X = H

14a R^2 = R^1 = Bz, X = Et_3SiO
14b R^2 = Bz, R^1 = H, X = Et_3SiO
14c R^2 = H, R^1 = Bz, X = Et_3SiO
14d R^2 = R^1 = H, X = Et_3SiO
15b R^2 = Bz, R^1 = X = H
15c R^2 = H, R^1 = Bz, X = H
15d R^2 = R^1 = X = H

5) We thank Dr. *Bruno Bernet* for a critical reassessment and correction of these data.

Table 1. *Cross-Coupling of 8-Iodoadenosine* **13** *with Heptynofuranosyl-adenine* **5**[a])

Entry	Catalyst[b])	Ligand[b])	Solvent	Temperature (Time)	Products and yields after separation
1	$(Ph_3P)_2PdCl_2$	none	Et_3N	r.t. (1 h) → 80° (3 h)	**14a**: 37%, **5:** 47%, **13:** 48%
2	$(Ph_3P)_2PdCl_2$	none	Et_3N	r.t. (1 h) → 80° (12 h)	**14a:** 17%
3	$(Ph_3P)_2PdCl_2$	none	5 equiv. Et_3N in DMF	r.t. (1 h) → 80° (12 h)	no reaction
4	$(Ph_3P)_2PdCl_2$	none	Et_3N/DMF 1 : 1	r.t. (1 h) → 80° (12 h)	no reaction
5	$(Ph_3P)_2PdCl_2$	none	pyrrolidine	r.t. 2 h	debenzoylation
6	$(Ph_3P)_2PdCl_2$	none	*N*-methylpyrrolidine	r.t. (1 h) → 70° (1 h)	**14a**: 46%
7	$(Ph_3P)_2PdCl_2$	none	$EtN(i\text{-}Pr)_2$	80° (5 h)	no reaction
8	$(Ph_3P)_2PdCl_2$	none	TMEDA	r.t. (1 h) → 80° (3 h)	**5**: 97%, **13**: decomposed
9	$(Ph_3P)_4Pd$	none	Et_3N	r.t. (1 h) → 80° (4 h)	**14a**: 25%, **5**: 53%, **13**: 69%
10	$Pd_2(dba)_3$	none	Et_3N	r.t. (1 h) → 80° (2 h)	**14a**: 70%
11	$Pd_2(dba)_3$	none	*N*-methylpyrrolidine	r.t. (1 h) → 70° (1 h)	**14a**: 44%
12	$(dppe)PdCl_2$	none	Et_3N	r.t. (1 h) → 80° (3 h)	no reaction
13	$(PhCN)_2PdCl_2$	none	Et_3N	r.t. (1 h) → 80° (3 h)	**14a**: 41%, **5**: 24%, **13**: 19%
14	$(MeCN)_2PdCl_2$	none	Et_3N	r.t. (1 h) → 80° (3 h)	**14a**: 23%, **5**: 57%, **13**: 69%
15	$Pd(OAc)_2$	$P(fur)_3$	Et_3N	r.t. (1 h) → 80° (1.5 h)	63%
16	$PdCl_2$	$P(fur)_3$	Et_3N	r.t. (1 h) → 80° (3 h)	**14a**: 58%, **5**: 13%, **13**: 16%
17	$Pd(acac)_2$	$P(fur)_3$	Et_3N	r.t. (1 h) → 80° (1 h)	**14a**: 63%
18	$Pd_2(dba)_3$	$P(fur)_3$	Et_3N	r.t. (1 h) → 80° (0.6 h)	**14a**: 89%
19	$Pd_2(dba)_3$	$P(C_6F_5)_3$	Et_3N	r.t. (1 h) → 80° (1.5 h)	**14a**: 69%
20	$Pd_2(dba)_3$	Bu_3P	Et_3N	r.t. (1 h) → 80° (3 h)	**14a**: 16%, **5**: 79%, **13**: 73%

[a]) Unless indicated otherwise, reactions were performed in the presence of 3 mol-% of the catalyst, 6 mol-% of the ligand, and 9 mol-% of CuI. [b]) dba = dibenzylideneacetone, dppe = 1,2-(diphenylphosphino)ethane, acac = acetylacetonate, fur = furan-2-yl.

Table 2. *Influence of the* N*-Benzoyl and the* Et_3SiO *Group on the Yield of the Cross-Coupling*[a])

Entry	8-Iodoadenosine	Acetylene	Solvent	Conditions	Product (yield [%])
1	**13**	**5**	Et_3N	r.t. (1 h) → 80° (40 min)	**14a** (89)
2	**13**	**6**	Et_3N	r.t. (2 h)	**14b** (83)
3	**3**	**5**	Et_3N	r.t. (1 h) → 80° (40 min)	**14c** (91)
4	**3**	**6**	Et_3N	r.t. (2 h)	**14d** (84)
5	**13**	**11**[b])	Et_3N	r.t. (1 h) → 80° (1 h)	no reaction
6	**13**	**12**	Et_3N	r.t. (5.5 h)	**15b** (60)
7	**3**	**11**[b])	Et_3N/toluene 1 : 1	r.t. (1 h) → 80° (1 h)	**15c** (71)
8	**3**	**12**	Et_3N	r.t. (5 h)	**15d** (78)

[a]) In the presence of 3 mol-% of $Pd_2(dba)_3$, 6 mol% of $P(fur)_3$, and 9 mol-% of CuI. Progress of the cross-coupling was monitored by observing the precipitation of triethylammonium hydroiodide. The end of the precipitation is correlated with the consumption of starting materials according to TLC. [b]) Compound **11** is poorly soluble in Et_3N.

also tested the influence of tertiary phosphines (*Entries 18–20*). Addition of 6 mol-% of tris(furan-2-yl)phosphine [17–21] accelerated the cross-coupling about threefold (*Entries 10* and *18*) and led to a rapid reaction that was terminated before any sizeable degradation of the dimer **14a** occurred. Coupling the free amines **3** and **6** under optimised conditions (*cf. Entry 18*) proceeded at room temperature over 2 h to yield 84% of **14d** (*Table 2*, *Entry 4*). Using these conditions, we compared the relation between the structure of the coupling partners and their reactivity (*Scheme 4*, *Table 2*).

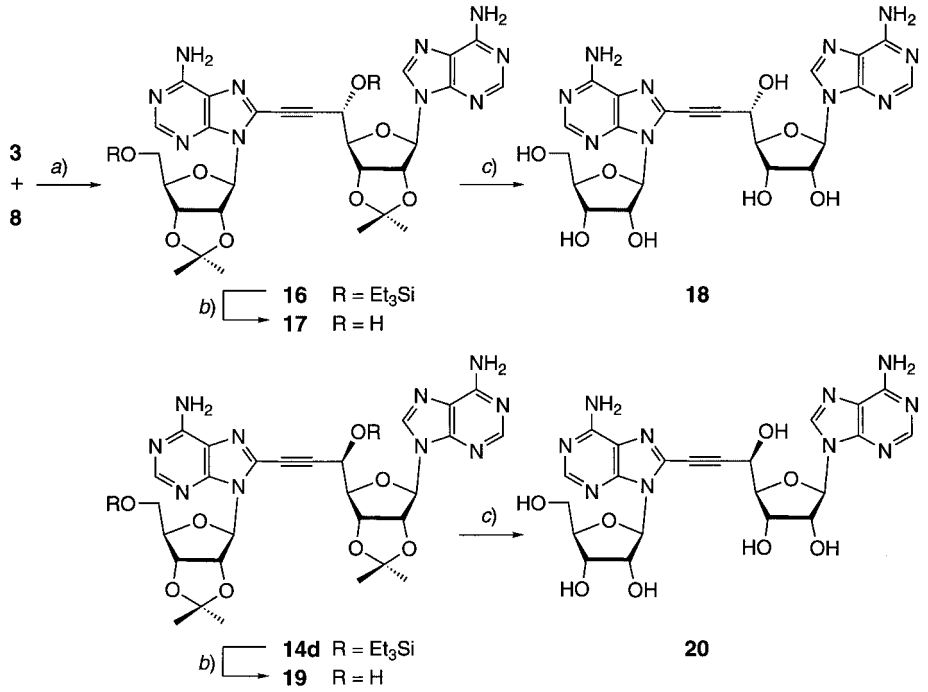
Inspection of *Table 2* shows that three substituents contribute to the reactivity and yields: the *N*-benzoyl and the Et_3SiO group of the acetylene, and the *N*-benzoyl group of the iodoadenosine. The amine **6** is more reactive than its *N*-benzoylated analogue **5**, as shown by the lower temperature required for the transformation of **13** and **3** (*Entries 2* and *4 vs. 1* and *3*); here the presence or absence of the *N*-benzoyl group in the iodoadenosine is irrelevant. Deoxygenation reduces the reactivity of the acetylene, as evidenced by comparing *Entries 5* and *7 vs. 1* and *3*, and *8* and *6 vs. 2* and *4*; again, the amine **12** is more reactive than the benzamide **11**. The results in *Entries 5* and *7* reflect the poor solubility of **11** in Et_3N; by changing the solvent to Et_3N/toluene 1:1 this problem is avoided for the reaction with the amine **3**, but not for the reaction with the benzamide **13**, which led at best to *ca.* 26% of the dimer (product not isolated). We assume that the required higher temperature reflects the lower reactivity rather than the influence of the solvent. Thus, the *N*-unsubstituted and *O*-silylated alkyne is the preferred partner for the cross-coupling.

As the NH_2 group in **6** is too far from the alkynyl group for a through-bond interaction, we rationalise the difference between the amines and benzamides by postulating that the more strongly basic adenyl residue in **6** co-ordinates at N(3) with the intermediate resulting from oxidative addition of the catalytically active $[PdL_2]$ species to the iodoadenosine and thereby promotes its interaction with the alkynyl moiety. The enhanced reactivity of the propargylic silyl ethers presumably correlates with the stronger acidity of the alkynyl group (*cf.* [17]), while the oxidative addition only becomes (marginally) relevant when the alkyne is particularly unreactive, as it is the case for the deoxygenated benzamide **11**. The approximate order of reactivity of the acetylene derivatives appears to be **6** > **12** > **5** > **11**.

The (5′*S*)-configured acetylene **8** showed the same reactivity as its epimer **6** (*Scheme 5*). Coupling **3** and **8** under standard conditions at room temperature for 2 h gave the dimer **16** in 76% yield. Desilylation of the protected dimers **14d** and **16** with aqueous AcOH in THF yielded 82 and 97% of the diols **17** and **19**, respectively. Finally, acidic hydrolysis of **17** and **19** in 80% HCOOH [2] led to the fully deprotected acetyleno-adenosine dimers **18** and **20** in 87 and 92% yield, respectively.

The assignment of the ^{1}H-NMR signals of the silyl ethers **14a**–**d**, **15b**–**d**, and **16** is based on 2D-COSY spectra of **14c**, **15c**, **15d**, and **16** (*Table 5* in the *Exper. Part*). As already observed for the monomers, N^6-debenzoylation leads to an upfield shift of H–C(2) ($\Delta\delta = 0.4-0.5$ ppm) and H–C(8) ($\Delta\delta = 0.1-0.2$ ppm). H–C(2/I) and H–C(2/II)[1]) of the dibenzamide **14a**, and the diamines **14d** and **15d** resonate at a similar field ($\Delta\delta$(H–C(2/I)/H–C(2/II) = 0.02–0.06 ppm). H–C(2′/II) of **14a**–**d**, **15b**–**d**, and **16** appears at 5.63–5.73 ppm. These compounds are *C*(8/II)-substituted adenosine derivatives and should therefore adopt the *syn*-conformation in unit II. The weak upfield shift of *ca.* 0.1 ppm of the H–C(2′) signal relative to one for H–C(2′) of the 8-iodoadenosine **3** probably reflects the influence of the different substituents and not an incomplete preference for the *syn*-conformation. H–C(2′/I) of **14a**–**d**, **15b**–**d**, and **16** appears at 5.41–5.64 ppm, 0.01–0.27 ppm upfield to the H–C(2′/II) signal in the same spectrum and 0.15–0.38 ppm downfield to H–C(2′) signal of the monomers **2**, **5**, **6**, and **8**, preferring the *anti*-conformation. These values suggest *anti* ⇌ *syn* equilibria between 7:3 to 1:3. Again, the *anti* ⇌ *syn* equilibria are paralleled by enhanced J(4′,5′) values of 5.7–7.3 Hz for **14a**–**d** and **15b**–**d** *vs.* 4.0–4.8 Hz for **2**, **5**,

Scheme 5

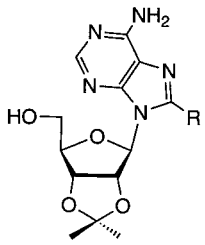


a) CuI, $[Pd_2(dba)_3]$, $P(fur)_3$, Et_3N; 76%. *b*) THF/AcOH/H_2O 1:2:1; 97% (**17**), 82% (**19**). *c*) 80% aq. HCO_2H; 92% (**18**), 87% (**20**).

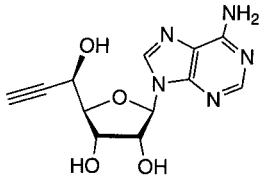
and **6**. In the absence of $^1H/^{13}C$-COSY spectra, an unambiguous assignment of the corresponding ^{13}C-NMR signals of unit I and unit II is not feasible. However, the shift difference for C(1′/I)/C(1′/II), C(2′/I)/C(2′/II), C(3′/I)/C(3′/II), and C(4′/I)/C(4′/II) of **14a**–**d**, **15b**–**d**, and **16** is small ($\Delta\delta < 2$ ppm, except for C(1′/I)/C(1′/II) of **16** (2.9 ppm) and C(4′/I)/C(4′/II) of **15b**–**d** (2.7–4.0 ppm); see *Exper. Part*). The *doublet* of C(5′/I) of **14a**–**d** and **16** appears at 63.5–64.4 ppm, the *triplet* of C(5′/I) of **15b**–**d** at 24.4–24.6 ppm, and the *triplet* of C(5′/II) of **14a**–**d**, **15b**–**d**, and **16** at 62.9–63.2 ppm. Ethynylation leads to the expected upfield shift[6]) of the *singlet* of C(8/II) of **14a**–**d**, **15b**–**d**, and **16** at 133.5–137.1 ppm as compared to the *doublet* of C(8/I) at 139.2–143.5 ppm. Two *singlets* of **14a**–**d**, **15b**–**d**, and **16** at 93.4–96.3 and at 71.3–75.5 ppm were assigned to C(6′/I) and C(7′/I), respectively, in agreement with the assignments for alkylated arylacetylenes [23].

The ^1H-NMR spectra of the diols **17** and **19** were recorded in (D_6)DMSO (*Table 5* in *Exper. Part*). The desilylation and the change of the solvent lead to an increase of $J(1',2')$ ($\Delta J \approx 1.5$ Hz), indicating a stronger preference of the 'southern' conformation by the diols in (D_6)DMSO than by the disilyl ethers in $CDCl_3$. As already observed for adenosine (**23a**) in DMSO [24][25], H–C(8/I) of **17** and **19** appears at lower field than

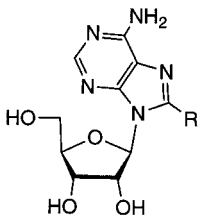
[6]) Ethynylation of benzene leads to an upfield shift of 6.2 ppm for the quaternary aromatic C-atom [22].



21a R = H
21b R = Me
21c R = Br



22



23a R = H
23b R = Et
23c R = Br

H–C(2/I) and H–C(2/II). This assignment is ascertained by the disappearance of the signal of **17** at 8.29 ppm upon iodination at C(8/I) [26]. A discussion of the *syn*/*anti*-conformation and the H-bonding of **17** and **19** in (D_6)DMSO requires reference data for the corresponding 8-unsubstituted and 8-substituted adenosines in the same solvent, as provided by **21a–c**. The 8-substituted adenosines **21b** [27] and **21c** [28] are expected to completely adopt a *syn*-conformation, whereas a 65:35 *syn* ⇌ *anti* equilibrium of the 8-unsubstituted **21a** in (D_6)DMSO has been deduced from NOE data [29]. The chemical shifts for H–C(2′) of **21a** (5.21 ppm [30]), **21b** (5.57 ppm [27]), and **21c** (5.68 ppm [7]) agree with this assignment. The presence of the 8-Br substituent leads to a stronger downfield shift similarly as observed for the iodide **3**. H–C(2′/II) of **17** (5.49 ppm) and **19** (5.40 ppm) resonate downfield to H–C(2′/I) at 5.32 and 5.36 ppm, respectively. A preference (> 75%) for the *syn*-conformation of all units of **17** and **19** is deduced from the δ(H–C(2′)) values of **21a–c**. The preference for the *syn*-conformation may be even more pronounced since the δ(H–C(2′)) values are also influenced by the intramolecular H-bond between HO–C(5′) and N(3). *O*(5′)-Unprotected 2′,3′-*O*-isopropylidene-adenosines form completely persistent intramolecular O(5′)–H···N(3) H-bonds in $CDCl_3$ solution (see [2][31] and refs. cit. therein). This H-bond leads to an upfield shift of 0.5–0.6 ppm for HO–C(2′) [2]. The change of the solvent from $CDCl_3$ to (D_6)DMSO reduces the persistence of the intramolecular H-bond in **21c**; the persistence is *ca.* 22%, as deduced from the *J*(4′,5′) values of 5.8 Hz [31]. The smaller *J*(4′,5′/II) values of 5.5 Hz of **17** and **19** suggest a *ca.* 32% persistence for the O(5′/II)–H···N(3/II) H-bond and, hence, probably a complete preference of the *syn*-conformation for unit II. The *J*(4′,5′/I) values of **17** and **19** are 5.5 and 6.5 Hz, respectively. An analogous analysis[7]) suggests a *ca.* 18% persistence for the O(5′/II)–H···N(3/II) H-bond of **19** and a *ca.* 45% persistence for the O(5′/II)–H···N(3/II) H-bond of **17** and, hence, a more or less complete preference for the *syn*-conformation also for unit I. The partially persistent O–H···N H-bonds are evidenced by the downfield shift of the OH signals: the primary HO–C(5′/II) resonates at 5.23 (**17**) and 5.15 ppm (**19**), and the secondary HO–C(5′/I) at 6.73 (**17**) and 6.65 ppm (**19**). The data have to be compared to δ(HO–C(5)) of pentofuranoses (4.55–4.69 ppm [32]) and hexofuranoses (4.43–4.69 ppm [32]). The persistence is also evidenced by the relatively large *J*(5′/I,OH) of **17** (6.8 *vs.* 11.0 Hz for a completely intramolecularly

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[7]) The limiting values for *J*(4′,5′/I) were taken from the ^{1}H-NMR spectra of *O*(5′)-unprotected and *O*(5′)-silylated 8-chloro-heptynofuranosyl-adenines (2.5 and 8.0 Hz for **17**, 2.0 and 7.5 Hz for **19** [2]).

H-bonded OH group [2], and *vs.* 3.5–5.5 Hz for a completely solvated secondary OH group [33]). A too rapid H,H-exchange leading to broad signals of the OH groups prevents a similar analysis of **19**.

The ^{1}H-NMR data of the fully deprotected dimers **18** and **20** in (D_6)DMSO/D_2O are compiled in *Table 3* together with the data of the related monomers: the propargyl alcohol **22** [2][8], adenosine (**23a**) [24][25], 8-ethyladenosine (**23b**) [27], and 8-bromoadenosine (**23c**) [34]. Adenosine (**23a**; $J(1',2') = 5.6$, $J(3',4') = 4.1$ Hz) slightly prefers a (*S*)-conformation, and the other compounds adopt a $^2T_3$ conformation, as evidenced by $J(1',2') = 6.5-7.8$ and $J(3',4') \leq 2.0$ Hz. Adenosine (**23a**) prefers to 60% the *syn*-conformation as determined by NOE measurements [29]. The 8-substituted derivatives **23b** and **23c** are expected to adopt completely the *syn*-conformation. Smaller $J(4',5')$ values are observed for **18**, **20**, **22**, and **23a–c** than for **17** and **19**, and indicate a stronger persistence of the intramolecular O(5′)–H···N(3) H-bond. The persistence calculated according to [31] increases from 50–52% (**23a**, **23c**, and unit II of **18** and **20**) to 55% (unit I of **20**), 72% (**22**), and 82% (unit I of **18**). H–C(2′/II) of **18** and **20** resonates at 4.91–4.93 ppm at a similar position as H–C(2) of 8-methyladenosine (**23b**), 0.1 ppm upfield to H–C(2) of 8-bromoadenosine (**23c**), and 0.3 ppm downfield to H–C(2) of adenosine (**23a**), evidencing a complete preference for the *syn*-conformation of unit II. Since unit I of **20** exhibits a similarly persistent H-bond as **23a** and **23c**, the δ(H–C(2′/I)) value of 4.72 ppm evidences a 80% preference for the *syn*-conformation. However, the persistence of the H-bond of **22** and unit I of **18** is higher by *ca.* 20–30% than that for **23a** and **23c**, leading to a significant upfield shift of the H–C(2′) signal[8]). Thus, the upfield shifts (4.63 and 4.68 ppm) still indicate a more

Table 3. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Deprotected Dimers* **18** *and* **20**, *and the Related Monomers* **22** *and* **23a–c** *in (D_6)DMSO/D_2O Solution*

	18 Unit I	**20** Unit I	**22** [2]	**18** Unit II	**20** Unit II	**23a** [24]	**23b** [27]	**23c** [7]
H–C(2)	8.13[a])	8.15[a])	8.14	8.15[a])	8.16[a])	8.15	8.07	8.12
H–C(8)	8.34	8.33	8.30	–	–	8.37	–	–
H–C(1′)	5.95	5.94	5.89	5.91	5.94	5.87	5.78	5.85
H–C(2′)	4.68	4.72	4.63	4.91	4.93	4.60	4.90	5.03
H–C(3′)	4.23	4.32	4.22	4.13–4.20	4.18	4.14	4.18	4.20
H–C(4′)	4.13–4.20	4.13	3.99	3.95	3.99	3.96	4.03	4.01
H_a–C(5′)	4.89	4.87	4.47	3.51	3.53	3.56	3.64	3.55
H_b–C(5′)	–	–	–	3.65	3.67	3.67	3.64	3.69
$J(1',2')$	7.0	7.5	7.8	6.5	6.5	5.6	7.1	7.0
$J(2',3')$	5.0	5.0	5.0	5.0	5.0	5.4	5.4	5.2
$J(3',4')$	2.0	1.0	<1	2.0	2.0	4.1	[b])	2.0
$J(4'a,5')$	3.5	4.5	3.5	3.5	3.5	3.6	[b])	3.5
$J(4'b,5')$	–	–	–	4.0	4.0	3.6	[b])	4.0
$J(5'a,5'b)$	–	–	–	12.5	12.5	12.2	[b])	12.5

[a]) Assignments may be interchanged. [b]) Not determined.

[8]) A 70% persistence of the intramolecular C(5′)–O···N(3) H-bond of **22** is also evidenced by the relatively small $J(5',OH) = 3.5$ Hz (*ca.* 1.5 Hz is expected for a completely persistent H-bond [2]) and by the downfield shift of HO–C(5′) resonating at 6.57 ppm [33]. No J(H,OH) and δ(OH) values are available for **18** and **20**.

or less complete preference for the *syn*-conformation. C(6′/I) and C(7′/I) of **18** and **20** appear at expected positions (94.5–95.4 and 70.4–70.7 ppm, resp.).

We thank the *Swiss National Science Foundation*, and *F. Hoffmann-La-Roche AG*, Basel for generous support.

Experimental Part

General. See [2]. *2′,3′*-O-*Isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**2**). At 25°, a soln. of **1** (*Fluka*, *puriss.*; 51.0 mg, 0.167 mmol) and imidazole (34.4 mg, 0.51 mmol) in dry DMF (1.5 ml) was treated dropwise with Et_3SiCl (84 µl, 0.50 mmol), stirred for 14 h, poured into ice-water (*ca.* 6 ml), and extracted with Et_2O/AcOEt 1:1 (3 × 3.0 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (2.5 g of silica gel; $CHCl_3$/acetone 1:1) gave **2** (48.7 mg, 70%). White solid. R_f ($CHCl_3$/acetone 1:1) 0.46. M.p. 110°. $[\alpha]_D^{25} = -49.7$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 260.0 (14000). IR ($CHCl_3$): 3413*m*, 2992*m*, 2959*s*, 2913*m*, 2878*m*, 1632*s*, 1589*s*, 1498*w*, 1416*m*, 1384*m*, 1376*m*, 1329*m*, 1295*m*, 1248*m*, 1156*m*, 1131*m*, 1089*s*, 1004*m*, 969*m*, 859*m*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.55 (q, $J = 7.9$, $(MeCH_2)_3Si$); 0.89 (t, $J = 7.9$, $(MeCH_2)_3Si$); 1.39, 1.63 (2*s*, Me_2C); 5.86 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5 (*s*, C(6)); 153.1 (*d*, C(2)); 149.5 (*s*, C(4)); 139.3 (*d*, C(8)); 120.0 (*s*, C(5)); 114.0 (*s*, Me_2C); 91.4 (*d*, C(1′)); 87.5 (*d*, C(4′)); 85.1 (*d*, C(2′)); 81.6 (*d*, C(3′)); 63.1 (*t*, C(5′)); 27.2, 25.4 (2*q*, Me_2C); 6.6 (*q*, $(MeCH_2)_3Si$); 4.1 (*t*, $(MeCH_2)_3Si$). FAB-MS: 422 ($[M+1]^+$). Anal. calc. for $C_{19}H_{31}N_5O_4Si$ (421.57): C 54.13, H 7.41, N 16.61; found: C 54.17, H 7.31, N 16.67.

Table 4. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Monomers* **2**, **3**, **5, 6**, *and* **8–12** *in $CDCl_3$ Solution*

	2	**3**	**10**	**11**	**12**	**5**	**6**	**8**	**9**
H–C(2)	8.37	8.22	8.86	8.79	8.36	8.84	8.36	8.37	8.88
H–C(8)	8.07	–	8.25	8.21	7.96	8.21	8.00	8.13	8.07
H–C(1′)	6.19	6.09	6.19	6.17	6.10	6.25	6.18	6.20	6.20
H–C(2′)	5.27	5.80	5.42	5.44	5.46	5.27	5.25	5.27	5.53
H–C(3′)	4.96	5.13	5.01	5.04	5.06	5.12	5.12	5.04	5.41
H–C(4′)	4.42	4.30	4.47	4.44	4.41	4.43	4.39	4.41	4.66
H_a–C(5′)	3.75	3.63	2.63	2.58	2.56	4.64	4.63	4.59	6.35
H_b–C(5′)	3.87	3.74	2.77	2.71	2.72	–	–	–	–
H–C(7′)	–	–	–	2.05	2.05	2.48	2.48	2.53	–
J(1′,2′)	2.5	2.0	2.8	2.8	2.5	3.0	3.0	2.3	2.0
J(2′,3′)	6.5	6.5	6.5	6.5	6.3	6.5	6.5	6.5	6.5
J(3′,4′)	2.5	3.5	2.8	3.0	3.0	2.5	2.5	2.0	3.0
J(4′,5′a)	4.0	6.5	5.5	5.8	6.0	4.5	4.8	5.5	8.5
J(4′,5′b)	4.0	6.5	6.0	6.7	7.0	–	–	–	–
J(5′a,5′b)	11.5	10.8	17.0	17.0	17.0	–	–	–	–
J(5′,7′)	–	–	–	2.7, 2.7	2.7, 2.7	2.0	2.2	2.3	–

8-Iodo-2′,3′-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosine* (**3**). A soln. of $^iPr_2NH$ (1.2 ml, 8.56 mmol) in dry THF (10.7 ml) was cooled to 0°, treated dropwise with 1.6M BuLi in hexane (5.3 ml, 8.48 mmol), stirred for 25 min, cooled to −78°, treated dropwise with a soln. of **2** (713.2 mg, 1.69 mmol) in dry THF (10.7 ml), stirred for 4 h, treated with I_2 (1.35 g, 5.32 mmol), stirred for 1 h, without cooling, and treated with sat. aq. NH_4Cl soln. and sat. aq. $Na_2S_2O_3$ soln. (10 ml each). The layers were separated, and the aq. layer was extracted with AcOEt (2 × 10 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (25 g of silica gel; $CHCl_3$/acetone 5:2) gave **3** (809.4 mg, 87%). Yellow solid. R_f ($CHCl_3$/acetone 5:2) 0.48. M.p. 68°. $[\alpha]_D^{25} = -11.9$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 266.0 (15000). IR ($CHCl_3$): 3411*w*, 2993*w*, 2958*m*, 2913*w*, 2876*m*, 1631*s*, 1584*m*, 1476*w*, 1456*w*, 1442*m*, 1415*w*, 1376*m*, 1317*w*, 1288*m*, 1157*m*, 1082*s*, 1005*m*, 972*w*, 915*w*, 873*w*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4;* additionally, 0.48 (q, $J = 8.0$, $(MeCH_2)_3Si$); 0.85 (t, $J = 8.0$,

(*Me*CH_2)$_3$Si); 1.39, 1.61 (2*s*, Me_2C); 5.92 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.4 (*s*, C(6)); 153.0 (*d*, C(2)); 150.8 (*s*, C(4)); 123.1 (*s*, C(5)); 114.2 (*s*, Me_2C); 100.8 (*s*, C(8)); 93.8 (*d*, C(1′)); 88.5 (*d*, C(4′)); 83.1 (*d*, C(2′)); 82.5 (*d*, C(3′)); 63.0 (*t*, C(5′)); 27.3, 25.5 (2*q*, *Me*$_2$C); 6.6 (*q*, (*Me*CH_2)$_3$Si); 4.2 (*t*, (Me*C*H_2)$_3$Si). FAB-MS: 548 ([$M+1$]$^+$). Anal. calc. for $C_{19}H_{30}IN_5O_4Si$ (547.47): C 41.68, H 5.52, N 12.79; found: C 41.82, H 5.68, N 12.71.

N^6-*Benzoyl-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5-O-(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**5**). At 25°, a soln. of **4** [2][8] (662.7 mg, 1.31 mmol) in dry THF (20 ml) was treated with a 1.0M soln. of Bu_4NF (TBAF) in THF (2.0 ml, 2.0 mmol), stirred for 3 h, and evaporated. FC (25 g of silica gel; $CHCl_3$/acetone 3:1) gave the propargylic alcohol (540.0 mg, 95%). At 25°, a soln. of this alcohol (1.1877 g, 2.73 mmol) and imidazole (550.8 mg, 8.09 mmol) in dry DMF (36 ml) was treated dropwise with Et_3SiCl (1.4 ml, 8.34 mmol), stirred for 12 h, poured into ice-water (*ca.* 60 ml), and extracted with hexane/AcOEt 1:1 (3 × 40 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (60 g of silica gel; hexane/AcOEt 1:2) gave **5** (1.3441 g, 90%). Light yellow solid. R_f (hexane/AcOEt 1:2) 0.46. M.p. 58–59°. $[\alpha]_D^{25} = +36.4$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 278.0 (18000). IR ($CHCl_3$): 3408*w*, 3305*w*, 2998*w*, 2958*w*, 2914*w*, 2878*w*, 2100*w*, 1709*m*, 1612*s*, 1585*s*, 1504*w*, 1479*m*, 1456*s*, 1404*w*, 1385*w*, 1356*w*, 1330*w*, 1295*w*, 1248*m*, 1156*w*, 1090*s*, 1003*w*, 972*w*, 948*w*, 867*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.64, 0.65 (2*q*, $J = 8.0$, (MeCH_2)$_3$Si); 0.93 (*t*, $J =$ 8.0, (*Me*CH_2)$_3$Si); 1.42, 1.65 (2*s*, Me_2C); 7.51 (*t*, $J = 7.8$, 2 arom. H); 7.60 (*t*, $J = 7.8$, 1 arom. H); 8.01 (*d*, $J = 7.8$, 2 arom. H); 9.08 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.9 (*s*, C=O); 153.2 (*d*, C(2)); 151.6 (*s*, C(6)); 149.9 (*s*, C(4)); 141.9 (*d*, C(8)); 134.0 (*s*); 133.0 (*d*); 129.1 (2*d*); 128.1 (2*d*); 123.5 (*s*, C(5)); 114.7 (*s*, Me_2C); 91.7 (*d*, C(1′)); 89.5 (*s*, C(4′)); 84.6 (*d*, C(2′)); 81.5 (*s*, C(6′)); 81.3 (*d*, C(3′)); 75.4 (*s*, C(7′)); 63.1 (*d*, C(5′)); 27.3, 25.5 (2*q*, *Me*$_2$C); 6.7 (*q*, (*Me*CH_2)$_3$Si); 4.7 (*t*, (Me*C*H_2)$_3$Si). FAB-MS: 550 ([$M+1$]$^+$). Anal. calc. for $C_{28}H_{35}N_5O_5Si \cdot 0.5\ H_2O$ (558.71): C 60.19, H 6.49, N 12.53; found: C 60.04, H 6.42, N 12.32.

9-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**6**). At 25°, a soln. of **4** (674.9 mg, 1.33 mmol) in MeOH (17 ml) was treated with 25% aq. NH_4OH (17 ml), stirred at 60° for 2 h, and evaporated. At 25°, a soln. of the crude residue in dry pyridine (22 ml) was treated dropwise with Et_3SiCl (0.67 ml, 3.99 mmol), stirred for 12 h, evaporated, and co-evaporated several times with PhMe. A soln. of the residue in $CHCl_3$ (40 ml) was washed with sat. aq. $NaHCO_3$ soln. (20 ml) and brine (10 ml), dried (Na_2SO_4), and evaporated. FC (20 g of silica gel; $CHCl_3$/acetone 1:1) gave **6** (536.5 mg, 91%). Light yellow solid. R_f ($CHCl_3$/acetone 2:3) 0.52. M.p. 57°. $[\alpha]_D^{25} = -66.7$ ($c = 1.04$, $CHCl_3$). UV ($CHCl_3$): 260.0 (130000). IR ($CHCl_3$): 3413*w*, 3305*m*, 2994*m*, 2959*m*, 2914*w*, 2878*w*, 2100*w*, 1632*s*, 1588*m*, 1506*w*, 1472*m*, 1417*w*, 1384*w*, 1375*m*, 1330*w*, 1296*w*, 1248*m*, 1156*w*, 1094*s*, 1004*w*, 972*w*, 904*w*, 863*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.64, 0.65 (2*q*, $J \approx 8.0$, (MeCH_2)$_3$Si); 0.94 (*t*, $J = 8.0$, (*Me*CH_2)$_3$Si); 1.41, 1.63 (2*s*, Me_2C); 5.91 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5 (*s*, C(6)); 153.2 (*d*, C(2)); 149.5 (*s*, C(4)); 139.3 (*d*, C(8)); 120.0 (*s*, C(5)); 114.3 (*s*, Me_2C); 91.2 (*d*, C(1′)); 89.3 (*d*, C(4′)); 84.4 (*d*, C(2′)); 81.7 (*s*, C(6′)); 81.2 (*d*, C(3′)); 75.0 (*s*, C(7′)); 63.0 (*d*, C(5′)); 27.2, 25.4 (2*q*, *Me*$_2$C); 6.7 (*q*, (*Me*CH_2)$_3$Si); 4.7 (*t*, (Me*C*H_2)$_3$Si). FAB-MS: 446 ([$M+1$]$^+$). Anal. calc. for $C_{21}H_{31}N_5O_4Si$ (445.59): C 56.61, H 7.01, N 15.72; found: C 56.45, H 7.09, N 15.48.

9-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]adenine* (**8**). At 25°, a soln. of **7** [2][8] (314.7 mg, 0.620 mmol) in MeOH (8.0 ml) was treated with 25% aq. NH_4OH (8.0 ml), stirred at 60° for 80 min, and evaporated. A soln. of the residue in dry pyridine (10 ml) was treated dropwise with Et_3SiCl (0.31 ml, 1.85 mmol) at 25°, stirred for 12 h, evaporated, and co-evaporated several times with PhMe. A soln. of the residue in $CHCl_3$ (35 ml) was washed with sat. aq. $NaHCO_3$ soln. (10 ml) and brine (7 ml), dried (Na_2SO_4), and evaporated. FC (15 g of silica gel; $CHCl_3$/acetone 1:2) gave **8** (184.1 mg, 67%). Light yellow solid. R_f ($CHCl_3$/acetone 1:2) 0.58. M.p. 142° (acetone/hexane). $[\alpha]_D^{25} = -10.0$ ($c = 1.01$, $CHCl_3$). UV ($CHCl_3$): 260.0 (13000). IR ($CHCl_3$): 3413*w*, 3304*w*, 2994*w*, 2958*m*, 2914*w*, 2878*w*, 2250*w*, 1632*s*, 1587*m*, 1498*w*, 1471*m*, 1415*w*, 1376*w*, 1330*w*, 1294*w*, 1248*w*, 1156*w*, 1131*m*, 1095*s*, 1004*m*, 908*w*, 867*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.48, 0.49 (2*q*, $J \approx 8.0$, (MeCH_2)$_3$Si); 0.84 (*t*, $J = 8.0$, (*Me*CH_2)$_3$Si); 1.40, 1.62 (2*s*, Me_2C); 5.92 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.5 (*s*, C(6)); 153.2 (*d*, C(2)); 149.4 (*s*, C(4)); 139.6 (*d*, C(8)); 120.1 (*s*, C(5)); 114.2 (*s*, Me_2C); 91.8 (*d*, C(1′)); 89.7 (*d*, C(4′)); 84.9 (*d*, C(2′)); 81.9 (*d*, C(3′)); 81.8 (*s*, C(6′)); 74.6 (*s*, C(7′)); 63.6 (*d*, C(5′)); 27.2, 25.4 (2*q*, *Me*$_2$C); 6.5 (*q*, (*Me*CH_2)$_3$Si); 4.4 (*t*, (Me*C*H_2)$_3$Si). FAB-MS: 446 ([$M+1$]$^+$). Anal. calc. for $C_{21}H_{31}N_5O_4Si$ (445.59): C 56.61, H 7.01, N 15.72; found: C 56.52, H 7.04, N 15.63.

N^6-*Benzoyl-9-[6,7-dideoxy-5*-O-*[(imidazol-1-yl)thiocarbonyl]-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-α*-L-talo-*hept-6-ynofuranosyl]adenine* (**9**). At 25°, a soln. of **7** (421.1 mg, 0.83 mmol) in dry CH_2Cl_2 (12.6 ml) was treated with (thiocarbonyl)diimidazole (289.2 mg, 1.62 mmol), stirred for 17 h, and evaporated. FC (25 g of silica gel; $CHCl_3$/acetone 2:1) gave **9**, which contained traces of impurities (369.5 mg, 72%). Yellow solid. R_f ($CHCl_3$/acetone 2:1) 0.46. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 4*; additionally, 0.24 (*s*, Me_3Si); 1.42, 1.63 (2*s*, Me_2C); 6.98–7.00 (*m*, 1 arom. H); 7.46–7.66 (*m*, 4 arom. H); 7.98–8.06 (*m*, 2 arom. H); 8.24 (br. *s*, 1 arom. H);

9.12 (br. *s*, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): 181.7 (*s*, C=S); 164.2 (*s*, C=O); 152.6 (*d*, C(2)); 150.6 (*s*, C(6)); 149.5 (*s*, C(4)); 142.0 (*d*, C(8)); 136.5 (*d*, C(2) of imidazolyl); 133.2 (*s*); 132.5 (*d*); 130.5 (*d*, C(5) of imidazolyl); 128.5 (2*d*); 127.5 (2*d*); 123.3 (*s*, C(5)); 117.7 (*d*, C(4) of imidazolyl); 114.4 (*s*, Me_2C); 96.2 (*s*, C(6′)); 95.8 (*d*, C(1′)); 91.2 (*s*, C(7′)); 87.5 (*d*, C(4′)); 83.6 (*d*, C(2′)); 81.8 (*d*, C(3′)); 72.4 (*d*, C(5′)); 26.6, 24.9 (2*q*, *Me*$_2$C); −0.8 (*s*, Me_3Si).

N^6-*Benzoyl-9-[5,6,7-trideoxy-2,3*-O-*isopropylidene-7*-C-*(trimethylsilyl)-β*-D-ribo-*hept-6-ynofuranosyl]adenine* (**10**). At 25°, a soln. of **9** containing traces of impurities (86.8 mg) in dry PhMe (2.6 ml) was treated with AIBN (2.8 mg, 17.1 μmol) and Bu_3SnH (74 μl, 0.28 mmol), stirred for 1 h at 80°, and evaporated. A soln. of the residue in MeCN (2 ml) was washed with hexane (2 × 2 ml) and evaporated. FC (4.5 g of silica gel; $CHCl_3$/AcOEt 1:1) and crystallization from AcOEt/hexane gave **10** (50.4 mg, 53% from **7**). White needles. R_f ($CHCl_3$/AcOEt 1:1) 0.47. M.p. 162°. $[\alpha]_D^{25} = -81.1$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 274.0 (17000). IR ($CHCl_3$): 3407*w*, 3007*m*, 2962*w*, 2176*w*, 1709*s*, 1612*s*, 1585*s*, 1504*w*, 1479*m*, 1456*s*, 1404*w*, 1385*m*, 1357*w*, 1328*m*, 1294*m*, 1252*s*, 1156*m*, 1087*s*, 1028*w*, 951*w*, 846*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 0.14 (*s*, Me_3Si); 1.42, 1.65 (2*s*, Me_2C); 7.54 (*t*, $J \approx 7.8$, 2 arom. H); 7.63 (*t*, $J \approx 7.8$, 1 arom. H); 8.03 (*d*, $J = 7.8$, 2 arom. H); 8.99 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.5 (*s*, C=O); 152.9 (*d*, C(2)); 151.2 (*s*, C(6)); 149.6 (*s*, C(4)); 141.8 (*d*, C(8)); 133.7 (*s*); 132.8 (*d*); 128.9 (2*d*); 127.9 (2*d*); 123.5 (*s*, C(5)); 114.7 (*s*, Me_2C); 101.5 (*s*, C(6′)); 91.4 (*s*, C(1′)); 87.9 (*s*, C(7′)); 84.6, 84.5 (2*d*, C(2′), C(4′)); 83.4 (*d*, C(3′)); 27.2, 25.4 (2*q*, *Me*$_2$C); 24.8 (*t*, C(5′)); 0.0 (*q*, Me_3Si). FAB-MS: 492 ($[M+1]^+$). Anal. calc. for $C_{25}H_{29}N_5O_4Si$ (491.62): C 61.08, H 5.95, N 14.25; found: C 61.14, H 5.91, N 14.08.

N^6-*Benzoyl-9-[5,6,7-trideoxy-2,3*-O-*isopropylidene-β*-D-ribo-*hept-6-ynofuranosyl]adenine* (**11**). At 25°, a soln. of **10** (55.3 mg, 0.112 mmol) in dry THF (1.7 ml) was treated with 1.0M soln. of TBAF in THF (0.17 ml, 0.17 mmol), stirred for 3 h, and evaporated. FC (2.0 g of silica gel; $CHCl_3$/AcOEt 3:4) gave **11** (47.1 mg, 100%). White solid. R_f ($CHCl_3$/AcOEt 1:2) 0.47. M.p. 78–79°. $[\alpha]_D^{25} = +52.3$ ($c = 1.02$, $CHCl_3$). 276.0 (15000). IR ($CHCl_3$): 3407*w*, 3307*m*, 3007*m*, 2940*w*, 2110*w*, 1708*s*, 1612*s*, 1585*s*, 1558*w*, 1540*w*, 1506*m*, 1480*m*, 1456*s*, 1419*w*, 1385*m*, 1359*w*, 1329*m*, 1248*s*, 1157*m*, 1089*s*, 1029*w*, 870*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 1.40, 1.63 (2*s*, Me_2C); 7.46–7.54 (*m*, 2 arom. H); 7.56–7.63 (*m*, 1 arom. H); 7.98–8.04 (*m*, 2 arom. H); 9.13 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.6 (*s*, C=O); 152.8 (*d*, C(2)); 151.2 (*s*, C(6)); 149.7 (*s*, C(4)); 142.1 (*d*, C(8)); 133.6 (*s*); 132.8 (*d*); 128.9 (2*d*); 127.9 (2*d*); 123.7 (*s*, C(5)); 114.8 (*s*, Me_2C); 91.2 (*d*, C(1′)); 85.0 (*d*, C(4′)); 84.4 (*d*, C(2′)); 83.4 (*d*, C(3′)); 79.4 (*s*, C(6′)); 71.1 (*s*, C(7′)); 27.2, 25.4 (2*q*, *Me*$_2$C); 23.4 (*t*, C(5′)). FAB-MS: 420 ($[M+1]^+$).

9-[5,6,7-Trideoxy-2,3-O-*isopropylidene-β*-D-ribo-*hept-6-ynofuranosyl]adenine* (**12**). At 25°, a soln. of **10** (143.0 mg, 0.291 mmol) in MeOH (3.6 ml) was treated with 25% aq. NH_4OH (3.6 ml), stirred at 60° for 1 h, and evaporated. FC (4.0 g of silica gel; $CHCl_3$/acetone 1:2) gave **12** (89.0 mg, 97%). White solid. R_f ($CHCl_3$/acetone 1:2) 0.46. M.p. 66°. $[\alpha]_D^{25} = -53.5$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 259.0 (10000). IR ($CHCl_3$): 3413*w*, 3307*m*, 2995*m*, 2100*w*, 1632*s*, 1588*m*, 1499*w*, 1473*m*, 1423*w*, 1384*m*, 1376*m*, 1330*m*, 1295*m*, 1248*m*, 1156*m*, 1095*s*, 1047*m*, 998*w*, 931*w*, 905*w*, 871*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 1.39, 1.61 (2*s*, Me_2C); 5.97 (br. *s*, NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0 (*s*, C(6)); 153.5 (*d*, C(2)); 149.6 (*s*, C(4)); 140.0 (*d*, C(8)); 120.5 (*s*, C(5)); 114.8 (*s*, Me_2C); 91.2 (*d*, C(1′)); 85.3 (*d*, C(4′)); 84.5 (*d*, C(2′)); 83.8 (*d*, C(3′)); 79.7 (*s*, C(6′)); 70.9 (*s*, C(7′)); 27.2, 25.4 (2*q*, *Me*$_2$C); 23.4 (*t*, C(5′)). FAB-MS: 316 ($[M+1]^+$).

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]adenine* (**14a**). At 25°, a soln. of **13** [2] (247.6 mg, 0.38 mmol) and **5** (209.1 mg, 0.38 mmol) in dry Et_3N (14 ml) was treated with CuI (7.6 mg, 39.9 μmol), P(fur)$_3$ (5.4 mg, 23.3 μmol) and $[Pd_2(dba)_3]$ (12.0 mg, 13.1 μmol), stirred for 1 h, warmed to 80°, stirred for 40 min, and evaporated. A soln. of the residue in $CHCl_3$ (20 ml) was washed with 2% aq. $Na_2(EDTA)$ soln. (2 × 10 ml), dried (Na_2SO_4), and evaporated. FC (20 g of silica gel; hexane/acetone 7:4) gave **14a** (362.6 mg, 89%). Light yellow solid. R_f (hexane/acetone 7:4) 0.48. M.p. 116°. $[\alpha]_D^{25} = -1.5$ ($c = 1.02$, $CHCl_3$). UV ($CHCl_3$): 292.0 (39000), 250.0 (29000). IR ($CHCl_3$): 3407*w*, 3006*m*, 2959*m*, 2913*w*, 2878*w*, 2230*w*, 1710*m*, 1610*s*, 1585*s*, 1511*w*, 1458*s*, 1422*w*, 1385*m*, 1330*m*, 1248*m*, 1157*w*, 1090*s*, 1004*w*, 972*w*, 869*w*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 0.49 (*q*, $J = 8.0$, $(MeCH_2)_3Si$); 0.725 (*q*, $J = 8.3$), 0.730 (*q*, $J = 7.8$) ($(MeCH_2)_3Si$); 0.86, 0.99 (2*t*, $J = 8.0$, 2 $(MeCH_2)_3Si$); 1.39, 1.43, 1.61, 1.65 (4*s*, 2 Me_2C); 7.42–7.53 (*m*, 4 arom. H); 7.53–7.62 (*m*, 2 arom. H); 7.98 (*d*, $J = 7.4$, 4 arom. H); 9.12, 9.22 (2 br. *s*, 2 NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.9 (*s*, 2 C=O); 153.7, 153.0 (2*d*, C(2/I), C(2/II)); 151.3, 150.6 (2*s*, C(6/I), C(6/II)); 150.1, 150.0 (2*s*, C(4/I), C(4/II)); 142.6 (*d*, C(8/I)); 136.7 (*s*, C(8/II)); 133.9 (2*s*); 133.0 (2*d*); 129.0 (4*d*); 128.1 (4*d*); 123.7 (*s*, C(5/I)); 123.0 (*s*, C(5/II)); 114.9, 114.3 (2*s*, 2 Me_2C); 96.0 (*s*, C(6′/I)); 91.2, 90.9 (2*d*, C(1′/I), C(1′/II)); 89.2, 88.4 (2*d*, C(4′/I), C(4′/II)); 84.3, 83.3 (2*d*, C(2′/I), C(2′/II)); 82.3, 81.6 (2*d*, C(3′/I), C(3′/II)); 74.6 (*s*, C(7′/I)); 63.6 (*d*, C(5′/I)); 63.0 (*t*, C(5′/II)); 27.20, 27.18, 25.46, 25.40 (4*q*, 2 *Me*$_2$C); 6.7, 6.6 (2*q*, 2 $(MeCH_2)_3Si$); 4.7, 4.2

Table 5. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Silyl Ethers* **14a**–**d**, **15b**–**d**, *and* **16** *in $CDCl_3$ and of the Diols* **17** *and* **19** *in (D_6)DMSO Solution*

	14a	**14b**	**14c**[a])	**14d**	**15b**	**15c**[a])	**15d**[a])	**16**[a])	**17**	**19**
H–C(2/I)	8.81[b])	8.29	8.83	8.28	8.29	8.81	8.28	8.46[b])	8.12[b])	8.13[b])
H–C(8/I)	8.25	8.04	8.28	8.15	8.10	8.27	8.17	8.29[b])	8.38	8.29
H–C(1′/I)	6.255	6.21	6.43	6.42	6.32	6.29	6.23	6.21	6.13	6.20
H–C(2′/I)	5.42	5.41	5.50	5.63	5.48	5.56	5.64	5.52	5.32	5.36
H–C(3′/I)	5.25	5.23	5.26	5.25	5.17	5.17	5.11	4.91	5.12	5.14
H–C(4′/I)	4.50	4.46	4.53	4.51	4.53	4.56	4.60	4.78	4.36	4.24
H–C(5′a/I)	4.96	4.95	4.96	4.79	2.96	2.99	2.92	4.86	4.90[d])	4.80[c])
H–C(5′b/I)	–	–	–	–	3.14	3.13	3.07	–	–	–
H–C(2/II)	8.79[b])	8.79	8.36	8.34	8.78	8.40	8.34	8.32[b])	8.19[b])	8.15[b])
H–C(1′/II)	6.245	6.27	6.19	6.21	6.15	6.25	6.27	6.27	6.23	6.02
H–C(2′/II)	5.69	5.68	5.63	5.64	5.68	5.62	5.66	5.73	5.49	5.40
H–C(3′/II)	5.15	5.15	5.12	5.14	5.15	5.14	5.16	5.20	4.98	4.92
H–C(4′/II)	4.29	4.29	4.25	4.27	4.31	4.29	4.31	4.32	4.09	4.10
H–C(5′a/II)	3.65	3.66	3.65	3.67	3.65	3.64	3.68	3.67	3.46[d])	3.42[c])
H–C(5′b/II)	3.77	3.77	3.75	3.78	3.76	3.74	3.74	3.79	3.55[d])	3.52[c])
J(1′,2′/I)	2.0	1.8	2.1	< 1	1.8	2.2	1.9	1.8	3.3	2.5
J(2′,3′/I)	6.5	6.5	6.3	6.5	6.5	6.3	6.3	6.0	6.0	6.2
J(3′,4′/I)	2.8	2.8	2.9	2.2	3.5	3.6	3.0	< 1	2.5	2.0
J(4′,5′a/I)	5.8	6.5	6.2	7.8	6.3	5.7	7.3	3.5	5.5	6.5
J(4′,5′b/I)	–	–	–	–	6.3	5.7	5.6	–	–	–
J(5′a,5′b/I)	–	–	–	–	17.7	17.4	17.4	–	–	–
J(1′,2′/II)	2.5	2.0	1.8	1.5	2.3	1.8	1.7	1.5	3.0	3.3
J(2′,3′/II)	6.5	6.5	6.3	6.5	6.5	6.3	6.3	6.5	6.5	6.0
J(3′,4′/II)	3.5	3.5	3.4	3.2	3.5	3.4	3.3	3.3	3.3	2.8
J(4′,5′a/II)	6.5	6.5	6.6	6.7	6.5	6.6	6.8	6.8	5.5	5.5
J(4′,5′b/II)	6.5	6.5	6.6	6.7	6.5	6.6	6.8	6.8	5.5	5.5
J(5′a,5′b/II)	10.5	10.5	10.6	10.5	10.5	10.6	10.3	10.5	13.5	12.5

[a]) Assignment based on a DQFCOSY.GRASP spectrum. [b]) Assignment may be interchanged. [c]) Line broadening due to coupling with OH group. [d]) J(5′a/I,OH) = 6.8, J(5′a/II,OH) = J(5′b/II,OH) ≈ 6.0 Hz.

(2*t*, 2 (Me*C*H$_2$)$_3$Si). FAB-MS: 1073 ([M + 1]$^+$). Anal. calc. for $C_{54}H_{68}N_{10}Si_2$ (1073.36): C 60.43, H 6.39, N 13.05; found: C 60.43, H 6.45, N 12.96.

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**14b**). At 25°, a soln. of **13** (51.1 mg, 79.0 μmol) and **6** (35.2 mg, 79.0 μmol) in dry Et$_3$N (2.6 ml) was treated with CuI (1.5 mg, 7.9 μmol), P(fur)$_3$ (1.1 mg, 4.7 μmol) and [Pd$_2$(dba)$_3$] (2.8 mg, 3.1 μmol), stirred for 2 h, and evaporated. A soln. of the residue in $CHCl_3$ (12 ml) was washed with 2% aq. Na$_2$(EDTA) soln. (2 × 5.0 ml), dried (Na$_2$SO$_4$), and evaporated. FC (4.0 g of silica gel; $CHCl_3$/acetone 7:4) gave **14b** (63.2 mg, 83%). White solid. R_f ($CHCl_3$/acetone 7:4) 0.46. M.p. 113°. $[\alpha]_D^{25} = +7.3$ (c = 1.01, $CHCl_3$). UV ($CHCl_3$): 317.0 (23000), 305.0 (32000), 253.0 (29000). IR ($CHCl_3$): 3412*w*, 2997*m*, 2958*m*, 2914*w*, 2878*m*, 2230*w*, 1710*m*, 1631*s*, 1608*s*, 1586*s*, 1510*w*, 1469*s*, 1423*m*, 1384*m*, 1376*m*, 1330*m*, 1266*m*, 1248*m*, 1157*m*, 1091*s*, 1004*m*, 972*m*, 870*m*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 0.49 (*q*, *J* = 8.0, (MeC*H*$_2$)$_3$Si); 0.717 (*q*, *J* = 8.3), 0.720 (*q*, *J* = 7.6) ((MeC*H*$_2$)$_3$Si); 0.87, 0.99 (2*t*, *J* = 8.0, 2 (*Me*CH$_2$)$_3$Si); 1.39, 1.42, 1.60, 1.63 (4*s*, 2 Me$_2$C); 5.95 (br. *s*, NH$_2$); 7.47 (*t*, *J* = 7.8, 2 arom. H); 7.57 (br. *t*, *J* = 7.8, 1 arom. H); 7.97 (*d*, *J* = 7.8, 2 arom. H); 9.37 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.8 (*s*, C=O); 155.6 (*s*, C(6/I); 153.5, 153.1 (2*d*, C(2/I), C(2/II)); 150.3 (*s*, C(6/II)); 149.7, 149.2 (2*s*, C(4/I), C(4/II)); 140.1 (*d*, C(8/I)); 136.5 (*s*, C(8/II)); 133.8 (*s*); 132.7 (*d*); 128.8 (2*d*); 127.9 (2*d*); 122.5, 120.1 (2*s*, C(5/I), C(5/II)); 114.5, 114.1 (2*s*, 2 Me$_2$*C*); 96.3 (*s* C(6′/I)); 91.0, 90.7 (2*d*, C(1′/I), C(1′/II)); 89.2, 88.2 (2*d*, C(4′/I), C(4′/II)); 84.1, 83.2 (2*d*, C(2′/I), C(2′/II)); 82.2, 81.7 (2*d*, C(3′/I), C(3′/II)); 74.2 (*s*, C(7′/I)); 63.5 (*d*, C(5′/I)); 62.9 (*t*, C(5′/II)); 27.15, 27.10, 25.5, 25.4 (4*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: 970 ([M + 1]$^+$). Anal. calc. for $C_{47}H_{64}N_{10}O_9Si_2$ (969.26): C 58.24, H 6.66, N 14.07; found: C 57.81, H 6.62, N 13.98.

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]adenine* (**14c**). According to the preparation of **14a**, treatment of **3** (74.5 mg, 0.136 mmol) with **5** (74.8 mg, 0.136 mmol) gave **14c** (119.7 mg, 91%). White solid. R_f ($CHCl_3$/acetone 3:2) 0.53. M.p. 121°. $[\alpha]_D^{25} = +8.5$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 284.0 (32000), 248.0 (13000). IR ($CHCl_3$): 3410*w*, 3208*w*, 3008*m*, 2959*m*, 2913*w*, 2878*m*, 2230*w*, 1709*m*, 1631*s*, 1613*s*, 1586*s*, 1506*w*, 1480*m*, 1456*s*, 1414*w*, 1384*m*, 1376*m*, 1328*m*, 1295*m*, 1248*s*, 1157*m*, 1087*s*, 1005*m*, 971*w*, 928*w*, 868*m*. ^{1}H-NMR (500 MHz, $CDCl_3$, assignment based on a DFQCOSY.GRASP spectrum): see *Table 5*; additionally, 0.49 (*q*, *J* = 7.9, (MeC*H*$_2$)$_3$Si); 0.741 (*q*, *J* = 8.2), 0.748 (*q*, *J* = 7.8) ((MeC*H*$_2$)$_3$Si); 0.86, 1.01 (2*t*, *J* = 7.9, 2 (*Me*CH$_2$)$_3$Si); 1.38, 1.44, 1.59, 1.66 (4*s*, 2 Me$_2$C); 6.63–6.80 (br. *s*, NH$_2$); 7.50 (*t*, *J* = 7.4, 2 arom. H); 7.59 (*t*, *J* = 7.5, 1 arom. H); 8.00 (*d*, *J* = 7.3, 2 arom. H); 9.09 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.8 (*s*, C=O); 156.1 (*s*, C(6/II)); 154.2, 153.0 (2*d*, C(2/I), C(2/II)); 151.1 (*s*, C(6/I)); 150.1, 148.9 (2*s*, C(4/I), C(4/II)); 143.5 (*d*, C(8/I)); 133.9 (2*s*, C(8/II), 1 arom. C); 133.0 (*d*); 129.1 (2*d*); 128.0 (2*d*); 123.7 (*s*, C(5/I)); 119.8 (*s*, C(5/II)); 114.8, 114.1 (2*s*, 2 Me$_2$*C*); 94.8 (*s*, C(6′/I)); 91.4, 90.7 (2*d*, C(1′/I), C(1′/II)); 90.1, 88.6 (2*d*, C(4′/I), C(4′/II)); 84.3, 83.6 (2*d*, C(2′/I), C(2′/II)); 82.6, 82.4 (2*d*, C(3′/I), C(3′/II)); 74.6 (*s*, C(7′/I)); 63.7 (*d*, C(5′/I)); 63.2 (*t*, C(5′/II)); 27.15, 27.10, 25.5, 25.4 (4*q*, 2 *Me*$_2$C); 6.7, 6.6 (2*q*, 2 (*Me*CH$_2$)$_3$Si); 4.8, 4.3 (2*t*, 2 (MeCH$_2$)$_3$Si). FAB-MS: 969 ([*M* + 1]$^+$).

2′,3′-O-*Isopropylidene-5′*-O-*(triethylsilyl)adenosin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]adenine* (**14d**). According to the preparation of **14b**, treatment of **3** (119.5 mg, 0.218 mmol) with **6** (97.2 mg, 0.218 mmol) gave **14d** (158.7 mg, 84%). White solid. R_f ($CHCl_3$/EtOH 10:1) 0.52. M.p. 119°. $[\alpha]_D^{25} = +59.2$ ($c = 1.06$, $CHCl_3$). UV ($CHCl_3$): 295.0 (20000), 266.0 (21000). IR ($CHCl_3$): 3412*w*, 3206*w*, 2993*m*, 2958*m*, 2914*w*, 2878*m*, 2230*w*, 1633*s*, 1588*m*, 1472*w*, 1415*w*, 1375*w*, 1328*m*, 1295*w*, 1248*w*, 1157*w*, 1090*s*, 1005*w*, 972*w*, 870*w*, 818*w*, 649*w*, 574*w*, 516*w*, 507*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 0.50 (*q*, *J* = 8.1, (MeC*H*$_2$)$_3$Si); 0.717 (*q*, *J* = 8.3), 0.720 (*q*, *J* = 7.6) ((MeC*H*$_2$)$_3$Si); 0.88, 0.99 (2*t*, *J* = 8.1, 2 (*Me*CH$_2$)$_3$Si); 1.38, 1.44, 1.59, 1.65 (4*s*, 2 Me$_2$C); 6.34 (br. *s*, NH$_2$); 6.80–7.22 (br. *s*, NH$_2$). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0, 155.9 (2*s*, C(6/I), C(6/II)); 153.8, 153.0 (2*d*, C(2/I), C(2/II)); 148.9, 148.7 (2*s*, C(4/I), C(4/II)); 140.5 (*s*, C(8/II)); 133.7 (*d*, C(8/I)); 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, 90.5 (2*d*, C(1′/I), C(1′/II)); 90.0, 88.4 (2*d*, C(4′/I), C(4′/II)); 84.0, 83.5 (2*d*, C(2′/I), C(2′/II)); 82.6, 82.5 (2*d*, C(3′/I), C(3′/II)); 74.3 (*s*, C(7′/I)); 63.5 (*d*, C(5′/I)); 63.1 (*t*, C(5′/II)); 27.1, 27.0, 25.4, 25.3 (4*q*, 2 *Me*$_2$C); 6.7, 6.6 (2*q*, 2 (*Me*CH$_2$)$_3$Si); 4.8, 4.2 (2*t*, 2 (MeCH$_2$)$_3$Si). FAB-MS: 865 ([*M* + 1]$^+$). Anal. calc. for $C_{40}H_{60}N_{10}O_8Si_2$ (865.15): C 55.53, H 6.99, N 16.19; found: C 55.29, H 6.93, N 15.99.

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-5′*-O-*(triethylsilyl)adenosin-8-yl-(8 → 7′)-9-(5,6,7-trideoxy-2,3*-O-*isopropylidene-β*-D-ribo-*hept-6-ynofuranosyl)adenine* (**15b**). According to the preparation of **14b**, treatment of **13** (182.3 mg, 0.280 mmol) with **12** (88.2 mg, 0.28 mmol; 5.5 h at r.t.) gave **15b** (141.5 mg, 60%). Light yellow solid. R_f ($CHCl_3$/acetone 2:3) 0.52. M.p. 128°. $[\alpha]_D^{25} = -44.2$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 304.0 (29000), 252.0 (28000). IR ($CHCl_3$): 3412*w*, 2997*m*, 2958*m*, 2877*w*, 2245*w*, 1710*m*, 1632*s*, 1609*s*, 1586*s*, 1151*w*, 1470*s*, 1424*m*, 1384*m*, 1376*m*, 1330*s*, 1248*s*, 1157*m*, 1089*s*, 1004*m*, 871*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 0.49 (*q*, *J* = 8.0, (MeC*H*$_2$)$_3$Si); 0.86 (*t*, *J* = 8.0, (*Me*CH$_2$)$_3$Si); 1.39 (br. *s*, 2 Me); 1.59, 1.63 (2*s*, 2 Me$_2$C); 6.08 (br. *s*, NH$_2$); 7.46 (*t*, *J* = 7.8, 2 arom. H); 7.56 (*t*, *J* = 7.8, 1 arom. H); 7.99 (*d*, *J* = 7.8, 2 arom. H); 9.49 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.0 (*s*, C=O); 155.6 (*s*, C(6/I)); 153.3, 153.1 (2*d*, C(2/I), C(2/II)); 150.3 (*s*, C(6/II)); 149.5, 149.1 (2*s*, C(4/I), C(4/II)); 140.2 (*d*, C(8/I)); 137.1 (*s*, C(8/II)); 133.8 (*s*); 132.7 (*d*); 128.7 (2*d*); 128.0 (2*d*); 122.5, 120.2 (2*s*, C(5/I), C(5/II)); 114.8, 114.1 (2*s*, 2 Me$_2$*C*); 95.4 (*s*, C(6′/I)); 90.6, 90.5 (2*d*, C(1′/I), C(1′/II)); 88.4, 84.4 (2*d*, C(4′/I), C(4′/II)); 84.3, 83.6 (2*d*, C(2′/I), C(2′/II)); 83.3, 82.2 (2*d*, C(3′/I), C(3′/II)); 71.3 (*s*, C(7′/I)); 62.9 (*t*, C(5′/II)); 27.2, 27.1, 25.41, 25.37 (4*q*, 2 *Me*$_2$C); 24.4 (*t*, C(5′/I)); 6.6 (*q*, (*Me*CH$_2$)$_3$Si); 4.2 (*t*, (MeCH$_2$)$_3$Si). FAB-MS: 839 ([*M* + 1]$^+$).

2′,3′-O-*Isopropylidene-5′*-O-*(triethylsilyl)adenosine-8-yl-(8 → 7′)*-N^6-*benzoyl-9-(2,3*-O-*isopropylidene-5,6,7-trideoxy-β*-D-ribo-*hept-6-ynofuranosyl)adenine* (**15c**). At 25°, a soln. of **3** (80.1 mg, 0.146 mmol) and **11** (61.4 mg, 0.146 mmol) in dry PhMe (2.1 ml) and dry Et_3N (2.1 ml) was treated with CuI (3.0 mg, 15.8 μmol), P(fur)$_3$ (2.0 mg, 8.6 μmol) and [Pd$_2$(dba)$_3$] (5.2 mg, 5.7 μmol), stirred for 1 h, warmed to 80°, stirred for 1 h, and evaporated. A soln. of the residue in $CHCl_3$ (16 ml) was washed with 2% aq. Na_2(EDTA) soln. (2 × 4.5 ml), dried (Na_2SO_4), and evaporated. FC (7.0 g of silica gel; $CHCl_3$/acetone 1:1) gave **15c** (90.9 mg, 71%). Light yellow solid. R_f ($CHCl_3$/EtOH 11:1) 0.43. M.p. 138°. $[\alpha]_D^{25} = -39.4$ ($c = 1.03$, $CHCl_3$). UV ($CHCl_3$): 283.0 (29000). IR ($CHCl_3$): 3411*w*, 2997*m*, 2957*w*, 2877*w*, 2245*w*, 1709*m*, 1631*s*, 1612*s*, 1586*m*, 1480*m*, 1456*s*, 1415*w*, 1384*m*, 1376*m*, 1328*m*, 1294*m*, 1248*m*, 1157*w*, 1086*s*, 1004*w*, 931*w*, 871*w*. ^{1}H-NMR (500 MHz, $CDCl_3$, assignment based on a DQFCOSY.GRASP spectrum): see *Table 5*; additionally, 0.49 (*q*, *J* = 7.9, (MeC*H*$_2$)$_3$Si); 0.86 (*t*, *J* = 7.9, (*Me*CH$_2$)$_3$Si); 1.38, 1.42, 1.59, 1.65 (4*s*, 2 Me$_2$C); 6.60–6.80 (br. *s*, NH$_2$); 7.51 (*t*, *J* = 7.6, 2 arom. H); 7.60 (*t*, *J* = 7.4, 1 arom. H); 7.99 (*d*, *J* = 7.4, 2 arom. H); 9.07 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.1 (*s*, C=O); 155.9 (*s*, C(6/II)); 154.1, 153.0 (2*d*, C(2/I), C(2/II)); 151.4 (*s*, C(6/I)); 150.1, 148.9 (2*s*, C(4/I), C(4/II));

143.2 (*d*, C(8/I)); 134.6 (*s*, C(8/II)); 133.9 (*s*); 133.0 (*d*); 129.0 (2*d*); 128.1 (2*d*); 123.9 (*s*, C(5/I)); 119.6 (*s*, C(5/II)); 115.3, 114.0 (2*s*, 2 Me_2C); 93.4 (*s*, C(6′/I)); 90.8, 90.6 (2*d*, C(1′/I), C(1′/II)); 88.7, 85.0 (2*d*, C(4′/I), C(4′/II)); 84.9, 83.7 (2*d*, C(2′/I), C(2′/II)); 83.6, 82.6 (2*d*, C(3′/I), C(3′/II)); 71.8 (*s*, C(7′/I)); 63.1 (*t*, C(5′/II)); 27.2 (*q*, 2 Me), 25.5, 25.4 (2*q*) (2 Me_2C); 24.4 (*t*, C(5′/I)); 6.6 (*q*, ($MeCH_2$)$_3$Si); 4.2 (*t*, ($MeCH_2$)$_3$Si). FAB-MS: 839 ($[M+1]^+$).

*2′,3′-*O*-Isopropylidene-5′-*O*-(triethylsilyl)adenosin-8-yl-(8 → 7′)-9-(5,6,7-trideoxy-2,3-*O*-isopropylidene-β-*D*-ribo-hept-6-ynofuranosyl)adenine* (**15d**). According to the preparation of **14b**, treatment of **3** (49.0 mg, 89.5 μmol) with **12** (28.2 mg, 89.4 μmol; 5 h at r.t.) gave **15d** (51.0 mg, 78%). Light yellow solid. R_f ($CHCl_3$/EtOH 6:1) 0.52. M.p. 133°. $[\alpha]_D^{25} = +39.5$ ($c = 1.03$, $CHCl_3$). UV ($CHCl_3$): 293.0 (22000), 266.0 (24000). IR ($CHCl_3$): 3412*m*, 3328*w*, 3201*w*, 2993*m*, 2958*m*, 2877*w*, 2245*w*, 1632*s*, 1588*m*, 1473*m*, 1416*w*, 1376*m*, 1329*m*, 1295*m*, 1248*m*, 1157*m*, 1086*s*, 1005*w*, 872*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, assignment based on a DQFCOSY.GRASP spectrum): see *Table 5*; additionally, 0.50 (*q*, $J = 8.0$, ($MeCH_2$)$_3$Si); 0.87 (*t*, $J = 7.9$, ($MeCH_2$)$_3$Si); 1.39, 1.42, 1.60, 1.64 (4*s*, 2 Me_2C); 6.35–6.50, 6.55–6.80 (2 br. *s*, 2 NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0, 155.7 (2*s*, C(6/I), C(6/II)); 153.7, 153.1 (2*d*, C(2/I), C(2/II)); 149.1, 148.7 (2*s*, C(4/I), C(4/II)); 140.0 (*d*, C(8/I)); 134.4 (*s*, C(8/II)); 120.2, 119.4 (2*s*, C(5/I), C(5/II)); 114.6, 113.8 (2*s*, 2 Me_2C); 93.5 (*s*, C(6′/I)); 91.2, 90.4 (2*d*, C(1′/I), C(1′/II)); 88.5, 85.0 (2*d*, C(4′/I), C(4′/II)); 84.3, 83.8 (2*d*, C(2′/I), C(2′/II)); 83.5, 82.5 (2*d*, C(3′/I), C(3′/II)); 71.6 (*s*, C(7′/I)); 63.0 (*t*, C(5′/II)); 27.2, 27.0 (2*q*), 25.4 (*q*, 2 Me) (2 Me_2C); 24.6 (*t*, C(5′/I)); 6.6 (*q*, ($MeCH_2$)$_3$Si); 4.2 (*t*, ($MeCH_2$)$_3$Si). FAB-MS: 735 ($[M+1]^+$).

*2′,3′-*O*-Isopropylidene-5′-*O*-(triethylsilyl)adenosin-8-yl-(8 → 7′)-9-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triethylsilyl)-α-L-talo-hept-6-ynofuranosyl]adenine* (**16**). According to the preparation of **14b**, treatment of **3** (170.9 mg, 0.312 mmol) with **8** (139.1 mg, 0.321 mmol) gave **16** (206.4 mg, 76%). White solid. R_f ($CHCl_3$/EtOH 10:1) 0.44. M.p. 122°. $[\alpha]_D^{25} = +143.6$ ($c = 1.00$, $CHCl_3$). UV ($CHCl_3$): 296.0 (21000), 266.0 (22000). IR ($CHCl_3$): 3467*w*, 3411*m*, 3338*w*, 3177*w*, 2993*m*, 2958*s*, 2913*m*, 2878*m*, 1633*s*, 1596*s*, 1472*m*, 1416*m*, 1384*m*, 1376*m*, 1328*s*, 1296*m*, 1248*m*, 1157*m*, 1130*s*, 1086*s*, 1005*m*, 912*w*, 868*m*, 824*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, assignment based on a DQFCOSY.GRASP spectrum): see *Table 5*; additionally, 0.45, 0.49 (2*q*, $J = 7.8$, 2 ($MeCH_2$)$_3$Si); 0.77, 0.87 (2*t*, $J = 7.9$, 2 ($MeCH_2$)$_3$Si); 1.41, 1.45, 1.61, 1.65 (4*s*, 2 Me_2C); 7.90–8.16 (br. *s*, 2 NH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.2, 156.1 (2*s*, C(6/I), C(6/II)); 154.0, 152.8 (2*d*, C(2/I), C(2/II)); 148.9, 148.8 (2*s*, C(4/I), C(4/II)); 139.2 (*d*, C(8/I)); 133.5 (*s*, C(8/II)); 119.9, 119.8 (2*s*, C(5/I), C(5/II)); 113.9, 113.8 (2*s*, 2 Me_2C); 94.4 (*s*, C(6′/I)); 93.6, 90.7 (2*d*, C(1′/I), C(1′/I)); 89.8, 88.7 (2*d*, C(4′/I), C(4′/II)); 85.5, 83.6 (2*d*, C(2′/I), C(2′/II)); 82.6, 82.3 (2*d*, C(3′/I), C(3′/II)); 75.5 (*s*, C(7′/I)); 64.4 (*d*, C(5′/I)); 63.1 (*t*, C(5′/II)); 27.2, 27.0, 25.4, 25.3 (4*q*, 2 Me_2C); 6.6, 6.5 (2*q*, 2 ($MeCH_2$)$_3$Si); 4.2, 4.1 (2*t*, 2 ($MeCH_2$)$_3$Si). FAB-MS: 865 ($[M+1]^+$).

*2′,3′-*O*-Isopropylideneadenosine-8-yl-(8 → 7′)-9-(6,7-dideoxy-2,3-*O*-isopropylidene-α-L-talo-hept-6-ynofuranosyl)adenine* (**17**). At 25°, a soln. of **16** (179.6 mg, 0.230 mmol) in 50% aq. THF (3.6 ml) was treated with AcOH (3.6 ml), stirred for 6.5 h, evaporated, and co-evaporated several times with PhMe. The residue was suspended in MeOH (2.0 ml), treated with SiO_2 (765 mg), evaporated, and the residue charged on a silica gel column. FC (12 g of silica gel; $CHCl_3$/MeOH 7:1) gave **17** (128.8 mg, 97%). Light yellow solid. R_f ($CHCl_3$/MeOH 7:1) 0.44. M.p. 166° (dec.). $[\alpha]_D^{25} = -62.3$ ($c = 0.82$, DMSO). UV (DMSO): 302.0 (19000), 268.0 (20000). IR (KBr): 3338*s*, 3188*s*, 2987*m*, 2936*m*, 2210*w*, 1646*s*, 1600*s*, 1577*s*, 1479*m*, 1425*m*, 1376*s*, 1330*s*, 1300*m*, 1269*m*, 1215*s*, 1156*m*, 1081*s*, 921*w*, 850*m*, 798*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 5*; additionally, 1.26, 1.34, 1.49, 1.57 (4*s*, 2 Me_2C); 3.40–3.60 (*m*, partially hidden by HDO signal, addn. of D_2O → 3.46/3.55, 2*dd*, $J = 13.5$, 5.5, 2 H–C(5′/II)); 4.90 (*t*, $J \approx 6.2$, addn. of D_2O → *d*, $J = 5.5$, H–C(5′/I)); 5.23 (*t*, $J \approx 6.0$, exchanged with D_2O, HO–C(5′/II)); 6.73 (*d*, $J = 6.8$, exchanged with D_2O, HO–C(5′/I)); 7.36 (br. *s*, exchanged with D_2O, NH_2); 7.61 (br. *s*, exchanged with D_2O, NH_2). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.0, 155.9 (2*s*, C(6/I), C(6/II)); 153.7, 152.5 (2*d*, C(2/I), C(2/II)); 148.5, 148.1 (2*s*, C(4/I), C(4/II)); 139.7 (*d*, C(8/I)); 132.1 (*s*, C(8/II)); 119.0, 118.8 (2*s*, C(5/I), C(5/II)); 113.4, 113.2 (2*s*, 2 Me_2C); 94.7 (*s*, C(6′/I)); 89.8, 89.5 (2*d*, C(1′/I), C(1′/II)); 87.6, 86.6 (2*d*, C(4′/I), C(4′/II)); 83.1, 82.0 (2*d*, C(2′/I), C(2′/II)); 81.2, 81.1 (2*d*, C(3′/I), C(3′/II)); 73.5 (*s*, C(7′/I)); 62.2 (*d*, C(5′/II)); 61.5 (*t*, C(5′/II)); 27.0, 26.9, 25.1, 25.0 (4*q*, 2 Me_2C). FAB-MS: 637 ($[M+1]^+$). Anal. calc. for $C_{28}H_{32}N_{10}O_8 \cdot 0.5\ H_2O$ (645.63): C 52.09, H 5.15, N 21.69; found: C 52.25, H 5.20, N 21.74.

Adenosin-8-yl-(8 → 7′)-9-(6,7-dideoxy-α-L-talo-hept-6-ynofuranosyl)adenine (**18**). At 25°, a soln. of **17** (89.0 mg, 0.14 mmol) in 80% aq. HCO_2H (4.5 ml) was stirred for 20 h, evaporated, and co-evaporated several times with PhMe. The residue was suspended in MeOH (3.0 ml), treated with reversed-phase SiO_2 (130 mg), evaporated, and the residue charged on a silica gel column. FC (4.0 g of reversed phase SiO_2; MeOH/H_2O 4:5) gave **18** (71.8 mg, 92%). White solid. R_f (BuOH/EtOH/H_2O 4:1:1) 0.46. M.p. 212° (dec.; 50% aq. MeOH). $[\alpha]_D^{25} = -5.0$ ($c = 0.73$, DMSO). UV (DMSO): 301.0 (19000), 269.0 (21000). IR (KBr): 3380*s*, 2932*m*, 2245*w*, 1652*s*, 1601*s*, 1578*m*, 1476*m*, 1422*m*, 1372*m*, 1331*s*, 1306*s*, 1273*m*, 1260*m*, 1212*m*, 1162*w*, 1125*s*, 1061*s*, 1034*s*, 984*m*, 903*w*, 846*w*, 796*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO/D_2O): see *Table 3*. ^{13}C-NMR (75 MHz, (D_6)DMSO):

156.1, 156.0 (2*s*, C(6/I), C(6/II)); 153.2, 152.3 (2*d*, C(2/I), C(2/II)); 148.8, 148.2 (2*s*, C(4/I), C(4/II)); 139.9 (*d*, C(8/I)); 133.0 (*s*, C(8/II)); 119.2, 119.1 (2*s*, C(5/I), C(5/II)); 95.4 (*s*, C(6′/I)); 89.2, 87.8 (2*d*, C(1′/I), C(1′/II)); 87.5, 86.5 (2*d*, C(4′/I), C(4′/II)); 73.0, 72.9 (2*d*, C(2′/I), C(2′/II)); 71.5, 70.8 (2*d*, C(3′/I), C(3′/II)); 70.7 (*s*, C(7′/I)); 62.0 (*d*, C(5′/I)); 61.9 (*t*, C(5′/II)). FAB-MS: 557 ($[M+1]^+$). Anal. calc. for $C_{22}H_{24}N_{10}O_8 \cdot 0.8\ H_2O$ (570.91): C 46.28, H 4.52, N 24.53; found: C 46.54, H 4.64, N 24.33.

*2′,3′-*O*-Isopropylideneadenosin-8-yl-(8→7′)-9-(6,7-dideoxy-2,3-*O*-isopropylidene-β-*D*-allo-hept-6-ynofuranosyl)adenine* (**19**). At 25°, a soln. of **14d** (175.6 mg, 0.230 mmol) in 50% aq. THF (3.5 ml) was treated with AcOH (3.5 ml), stirred for 8 h, evaporated, and co-evaporated several times with PhMe. A suspension of the residue in MeOH (2.0 ml) was treated with SiO_2 (400 mg), evaporated, and the residue charged on a silica gel column. FC (6.0 g of silica gel; $CHCl_3$/MeOH 8:1) gave **19** (105.5 mg, 82%). White solid. R_f ($CHCl_3$/MeOH 8:1) 0.38. M.p. 167° (dec.). $[\alpha]_D^{25} = +1.6$ ($c = 1.07$, DMSO). UV (DMSO): 303.0 (19000), 271.0 (19000). IR (KBr): 3333*s*, 3192*s*, 2987*m*, 2937*m*, 2210*w*, 1651*s*, 1599*s*, 1576*s*, 1479*m*, 1456*m*, 1420*w*, 1376*s*, 1329*s*, 1301*m*, 1268*m*, 1215*s*, 1156*m*, 1082*s*, 970*w*, 852*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 5*; additionally, 1.26, 1.32, 1.47, 1.53 (4*s*, 2 Me_2C); 5.15 (br. *s*, exchanged with D_2O, HO–C(5′/II)); 6.65 (br. *s*, exchanged with D_2O, HO–C(5′/I)); 7.35 (br. *s*, exchanged with D_2O, NH_2); 7.59 (br. *s*, exchanged with D_2O, NH_2). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.4, 156.3 (2*s*, C(6/I), C(6/II)); 154.0, 152.9 (2*d*, C(2/I), C(2/II)); 148.8, 148.4 (2*s*, C(4/I), C(4/II)); 140.1 (*d*, C(8/I)); 132.3 (*s*, C(8/II)); 119.2, 119.0 (2*s*, C(5/I), C(5/II)); 113.5 (*s*, 2 Me_2C); 95.2 (*s*, C(6′/I)); 89.9, 89.8 (2*d*, C(1′/I), C(1′/II)); 88.0, 86.6 (2*d*, C(4′/I), C(4′/II)); 83.4, 82.1 (2*d*, C(2′/I), C(2′/II)); 81.5 (*d*, C(3′/I), C(3′/II)); 73.6 (*s*, C(7′/I)); 61.8 (*d*, C(5′/I)); 61.6 (*t*, C(5′/II)); 27.0, 26.9, 25.18, 25.14 (4*q*, 2 Me_2C). FAB-MS: 637 ($[M+1]^+$). Anal. calc. for $C_{28}H_{32}N_{10}O_8$ (636.62): C 52.83, H 5.07, N 22.00; found: C 52.88, H 5.26, N 22.07.

*Adenosin-8-yl-(8→7′)-9-(6,7-dideoxy-β-*D*-allo-hept-6-ynofuranosyl)adenine* (**20**). At 25°, a soln. of **19** (117.1 mg, 0.184 mmol) in 80% aq. HCO_2H (3.5 ml) was stirred for 14 h, evaporated, and co-evaporated several times with PhMe. A suspension of the residue in MeOH (4.0 ml) was treated with reversed-phase SiO_2 (200 mg), evaporated, and the residue charged on a silica gel column. FC (5.0 g of reversed phase SiO_2; MeOH/H_2O 1:1) gave **20** (89.0 mg, 87%). White solid. R_f (BuOH/EtOH/H_2O 4:1:1) 0.50. M.p. 168° (dec.; 50% aq. MeOH). $[\alpha]_D^{25} = -84.4$ ($c = 1.05$, DMSO). UV (DMSO): 301.0 (17000), 271.0 (17000). UV (H_2O): 296 (20000), 264 (25000), 231 (27000), 209 (30000). IR (KBr): 3331*s*, 2921*m*, 1657*s*, 1604*s*, 1577*m*, 1483*m*, 1424*m*, 1332*s*, 1309*m*, 1253*m*, 1220*m*, 1084*s*, 1060*s*, 879*w*, 844*w*, 796*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO/D_2O): see *Table 3*. ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.1, 156.0 (2*s*, C(6/I), C(6/II)); 153.3, 152.3 (2*d*, C(2/I), C(2/II)); 149.0, 148.2 (2*s*, C(4/I), C(4/II)); 139.9 (*d*, C(8/I)); 132.9 (*s*, C(8/II)); 119.1 (*s*, C(5/I), C(5/II)); 94.5 (*s*, C(6′/I)); 89.3, 87.5 (2*d*, C(1′/I), C(1′/II)); 87.4, 86.6 (2*d*, C(4′/I), C(4′/II)); 73.6, 72.9 (2*d*, C(2′/I), C(2′/II)); 71.6, 70.9 (2*d*, C(3′/I), C(3′/II)); 70.4 (*s*, C(7′/I)); 62.3 (*d*, C(5′/I)); 62.1 (*t*, C(5′/II)). FAB-MS: 557 ($[M+1]^+$). Anal. calc. for $C_{22}H_{24}N_{10}O_8 \cdot H_2O$ (574.51): C 45.99, H 4.56, N 24.38; found: C 46.23, H 4.47, N 24.04.

REFERENCES

[1] S. Eppacher, N. Solladié, B. Bernet, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1311.
[2] H. Gunji, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1331.
[3] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *50*, 4467.
[4] J. Tomasz, *Nucleic Acid Chem.* **1978**, *2*, 765.
[5] H. Hayakawa, K. Haraguchi, H. Tanaka, T. Miyasaka, *Chem. Pharm. Bull.* **1987**, *35*, 72.
[6] H. Hayakawa, H. Tanaka, K. Sasaki, K. Haraguchi, T. Saitoh, F. Takai, T. Miyasaka, *J. Heterocycl. Chem.* **1989**, *26*, 189.
[7] H. Gunji, A. Vasella, unpublished results.
[8] A. Matsuda, H. Kosaki, Y. Saitoh, Y. Yoshimura, N. Minakawa, H. Nakata, *J. Med. Chem.* **1998**, *41*, 2676.
[9] T. D. W. Claridge, 'High-Resolution NMR Techniques in Organic Chemistry', in 'Tetrahedron Organic Chemistry Series', Eds. J. E. Baldwin, F. R. S. Williams, and M. Williams, Pergamon, Amsterdam, 1999, Vol. 19, p. 142.
[10] R. Bürli, A. Vasella, *Helv. Chim. Acta* **1999**, *82*, 485.
[11] W. Höbold, R. Radeglia, D. Klose, *J. Prakt. Chem.* **1976**, *318*, 519.
[12] M. I. Al-Hassan, I. M. Al-Najjar, I. M. Al-Oraify, *Magn. Reson. Chem.* **1989**, *27*, 1112.
[13] G. C. Levy, D. M. White, J. D. Cargioli, *J. Magn. Reson.* **1972**, *8*, 280.
[14] S. Manfredini, P. G. Baraldi, R. Bazzanini, M. Marangoni, D. Simoni, J. Balzarini, E. De Clercq, *J. Med. Chem.* **1995**, *38*, 199.

[15] R. M. Moriarty, W. R. Epa, A. K. Awasthi, *Tetrahedron Lett*. **1990**, *31*, 5877.
[16] M. Alami, F. Ferri, G. Linstrumelle, *Tetrahedron Lett*. **1993**, *34*, 6403.
[17] C. Cai, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 2053.
[18] R. Bürli, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 1027.
[19] R. Bürli, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 2215.
[20] T. V. Bohner, R. Beaudegnies, A. Vasella, *Helv. Chim. Acta* **1999**, *82*, 143.
[21] T. V. Bohner, O. Becker, A. Vasella, *Helv. Chim. Acta* **1999**, *82*, 198.
[22] E. Pretsch, T. Clerc, J. Seibl, W. Simon, 'Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden', Springer-Verlag, Berlin, 1990, p. C120.
[23] P. A. A. Klusener, J. C. Hanekamp, L. Brandsma, P. von Rague-Schleyer, *J. Org. Chem*. **1990**, *55*, 1311.
[24] Y. Komoda, Y. Isogai, K. Satoh, *Chem. Pharm. Bull*. **1983**, *31*, 2771.
[25] M. Liu, R. D. Farrant, J. M. Gillam, J. K. Nicholson, J. D. Lindon, *J. Magn. Reson., Ser. B* **1995**, *109*, 275.
[26] K. B. Punit, A. Vasella, unpublished results.
[27] T. Ueda, Y. Nomoto, A. Matsuda, *Chem. Pharm. Bull*. **1985**, *33*, 3263.
[28] M. Ikehara, S. Uesugi, K. Tomita, *Nucleic Acid Chem*. **1978**, *2*, 837.
[29] H. Rosemeyer, G. Toth, B. Golankiewicz, Z. Kazimierczuk, W. Bourgeois, U. Kretschmer, H. P. Muth, F. Seela, *J. Org. Chem*. **1990**, *55*, 5784.
[30] L. Poppe, W. E. Hull, J. Retey, *Helv. Chim. Acta* **1993**, *76*, 2367.
[31] L. H. Koole, H. de Boer, J. W. de Haan, C. A. G. Haasnoot, P. van Dael, H. M. Buck, *J. Chem. Soc.*, *Chem. Commun*. **1986**, 362.
[32] S. J. Angyal, J. C. Christofides, *J. Chem. Soc., Perkin Trans. 2* **1996**, 1485.
[33] B. Bernet, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 995.
[34] T. P. Prakash, R. Kumar, K. N. Ganesh, *Tetrahedron* **1993**, *49*, 4035.

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