Oligonucleosides with a Nucleobase-Including Backbone

Part 7

syn and *anti* Conformations of a (5′–8)-Ethynediyl-Linked Adenosine Dimer

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The conformational analysis of **7** was carried out in (D_6)DMSO and in mixtures of (D_6)DMSO and $CDCl_3$ to evaluate the *syn*/*anti* conformations, relevant to the pairing propensity of this type of nucleotide analogue. The HO–C(5′) of unit I and of unit II of the dimer **7** form an intramolecular H-bond to N(3). In (D_6)DMSO, the C(5′)–OH···N(3) H-bond in unit I is partially broken, while that in unit II persists to a larger extent. The *syn* conformation prevails for unit I and particularly for unit II. The furanosyl moieties adopt predominantly a 2′-*endo* conformation that is largely independent of the solvent.

Introduction. – In spite of extensive modifications of oligonucleotides, all known analogues are of type **A** (*Fig.*) *i.e.*, they maintain the structural entities of backbone and nucleobase [1]. This has led to the question of whether this structural invariant is a necessary prerequisite for the formation of homo and/or hetero duplexes. To answer this question, we have designed oligonucleotide analogues of type **B** (*Fig.*) that do not differentiate between backbone and nucleobase[1]). The representatives **1** and **2** of this type of oligonucleotide analogues (*Fig.*) were considered capable of forming duplexes[2]). An ethynediyl-linked uridine-derived hexamer **1** ($n=4$) [2] and an analogous adenosine-derived tetramer **2** ($n=2$) [3] have been synthesized. These oligomers did not pair; they may be too short. Before synthesizing longer oligomers, we wanted to analyse the conformations of a simple representative of **2**. The preferred conformation of oligonucleotides is an essential factor determining their pairing ability; and the preferred conformation of polynucleotides corresponds to that of the related mononucleosides and mononucleotides [4–8].

The *anti* conformation [9] is a prerequisite for pairing of DNA and RNA [10–12]; it appears to be also required for the pairing of type **1** and **2** oligomers of C(8)-substituted purine and C(6)-substituted pyrimidine units [2]. Although it is known that at least some C(8)-substituents on purines and C(6)-substituents on pyrimidines induce a *syn* conformation [13], we speculated that the sterically undemanding alkynyl substituent may be compatible with a significant population of an *anti* conformation. It has been reported that a single 2′-deoxy-8-(prop-1-yn-1-yl)adenosine moiety in an oligodeoxynucleotide hybridises with the corresponding base in the complementary strand, albeit (in this case) not as well as the unmodified adenosine moiety [14]. This suggests that

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[1]) For the sake of simplicity, we have designated these analogues as 'oligonucleotide analogues with a nucleobase-including backbone', while, strictly speaking, these new systems do not possess a 'backbone'.

[2]) According to *Maruzen* model studies and *Macromodel* calculations using the Amber* force-field [2].

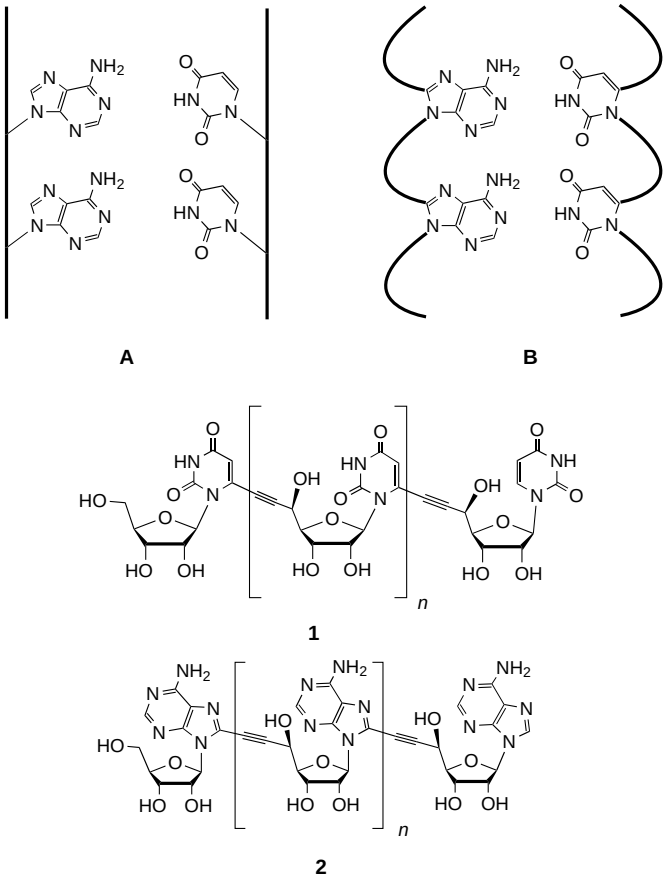
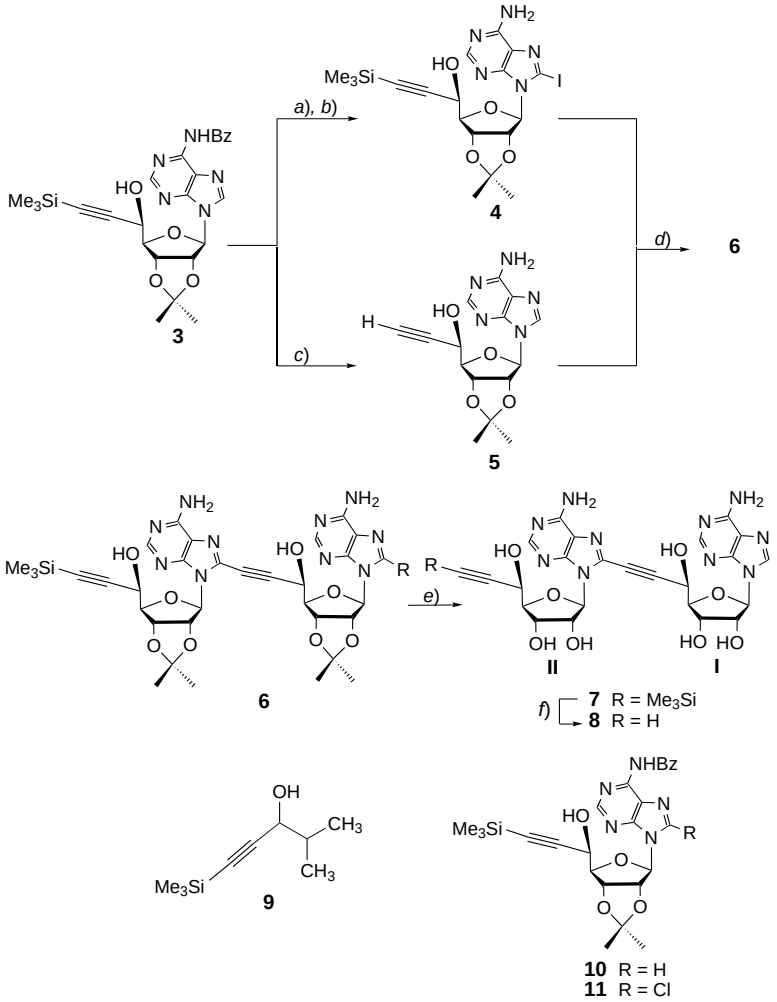


Figure. *Schematic representation of backbone and nucleobases of known oligonucleotides and analogues* (**A**), *oligonucleotides with a nucleobase-including backbone* (**B**), *and ethynediyl-bridged uridine* (**1**) *and adenosine* (**2**) *oligomers with a nucleobase-including backbone*

such a *C*(8)-alkynylated adenosine moiety can adopt a (somewhat disfavoured) *anti* conformation for pairing. The propensity for hybridisation is also influenced by the conformation of the ribosyl ring and the orientation of the substituent at C(4′) [15][16]. The rotation about the C(1′)–N(9) and C(4′)–C(5′) bonds is influenced by the intramolecular H-bond from HO–C(5′) to N(3) of purines [17–24]. This H-bond is incompatible with the *anti/gt* conformation that appears to be required for pairing of analogues **1** and **2** [2].

The increased acidity of the propargylic HO–C(5′) group in monomeric *C*(5′)-alkynylated analogues of adenosine favours the C(5′)–OH···N(3) H-bond [17][24]. To see if this H-bond is similarly favoured in analogues of type **2**, we intended to analyse the conformation of the dimer **7** (*Scheme*), the silylated analogue of the simplest representative of the oligoadenosines **2**. The dimer **7** has the advantage of combining C(8)-substituted and C(8)-unsubstituted adenosyl moieties (units I and II),

Scheme



a) LDA, THF; then NIS. *b*) $MeNH_2$, THF; 75%. *c*) THF, $MeNH_2$; Bu_4NF, THF; 70%. *d*) [$Pd_2(dba)_3$], CuI, $P(fur)_3$, toluene/Et_3N 1:1; 86%. *e*) CF_3CO_2H/H_2O 1:2, THF; 88%. *f*) $Bu_4NF \cdot 3\,H_2O$, THF; 54%.

the unsubstituted adenosyl moiety corresponding to unit I, allowing assessment of the effect of the C(8)-substituent of unit II.

Results and Discussion. – 1. *Synthesis.* The dimer **7** (*Scheme*) was prepared from adenosine *via* **3** [24], which served as common intermediate for the synthesis of the iodo derivative **4** and the alkyne **5** (*cf.* [3][25]). Iodination of **3** followed by debenzoylation provided **4** in 75% yield, while debenzoylation of **3** followed by desilylation yielded 70% of **5**. *Sonogashira* coupling [25] of **4** and **5** to **6** (86%) followed by deprotection of

the product by treatment with trifluoroacetic acid gave **7** (88%) as a solid that decomposes at 180° and that is poorly soluble in H_2O and MeOH, but soluble in DMSO, mixtures of $CDCl_3$ and at least 21% of DMSO, and in a *ca.* 8:2 mixture of $CHCl_3$ and MeOH. Treatment of **7** with tetrabutylammonium fluoride afforded the desilylated dimer **8** (54%). The propargyl alcohol **9** was synthesized as described by *Kitano et al.* [26].

2. *Conformational Analysis.* The ^{1}H-NMR spectra of **7** were recorded in (D_6)DMSO and in $CDCl_3$ containing increasing amounts of (D_6)DMSO. As described below, the minimal content of (D_6)DMSO in $CDCl_3$ ensuring solubility of **7** (21%) is sufficiently low to allow detection and analysis of the intramolecular H-bonds of interest, while higher amounts of DMSO are expected to disrupt weak H-bonds and to impair H-bonds of medium strength [27][28].

The ^{1}H-NMR signals of **7** in (D_6)DMSO (*Table 1*) were assigned as follows. The *s*'s at 8.34, 8.16, and 8.13 ppm resonating at lowest fields were assigned to one of H–C(8/I), H–C(2/I), or H–C(2/II). Exchange with D_2O showed that the signals at 7.72, 7.38, 7.02, 6.90, 5.52, 5.47, 5.39, and 5.38 ppm correspond to six OH and two NH_2 groups, the broad *s*'s at 7.72 and 7.38 integrating for two H each and thus corresponding to NH_2 groups. Upon addition of D_2O, the H–C *ddd*'s at 4.91, 4.75, 4.33, and 4.29 ppm changed to *dd*'s and the broad H–C *t*'s at 4.89 and 4.55 ppm to *d*'s. These findings and the analogy to related monomers [24] evidence that the *ddd*'s at 4.91 ($J = 7.5$, 6.5, and 5.2 Hz) and 4.75 ppm ($J = 7.8$, 6.5, and 5.4 Hz) correspond to H–C(2′), those at 4.33 ($J = 5.4$, 3.2, and 1.0 Hz) and 4.29 ppm ($J = 5.3$, 3.1, and 1.2 Hz) to H–C(3′), and the *t*'s at 4.89 and 4.55 ppm to H–C(5′). The *d*'s at 5.95 ($J = 7.8$ Hz) and 5.96 ($J = 7.5$ Hz), and the *dd*'s at 4.14 ($J = 4.3$, 1.0) and 4.00 ($J = 3.4$, 1.2) did not change upon addition of D_2O; the former were assigned to H–C(1′) and the latter to H–C(4′) of the two units.

Table 1. *^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of* **7** *in Varying Concentrations of (D_6)DMSO in $CDCl_3$*

Amount of (D_6)DMSO	21%		28%		40%		60%		80%		100%	
	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II
H–C(2)	8.13	8.08	8.12	8.08	8.13 [a])	8.11 [a])	8.14 [a])	8.13 [a])	8.19 [a])	8.13 [a])	8.16	8.13
H–C(8)	8.01	–	8.03	–	8.07 [a])	–	8.24 [a])	–	8.26 [a])	–	8.34	–
H–C(1′)	5.89	6.08	5.90	6.07	5.94	6.04	5.95	6.00	5.96	6.00	5.95	5.96
H–C(2′)	4.70	4.77	4.71	4.77	4.69	4.77	4.71	4.81	4.72	4.83	4.75	4.91
H–C(3′)	4.55	4.40	4.54	4.39	4.46	4.34	4.39	4.30	4.36	4.32	4.33	4.29
H–C(4′)	4.33	4.18	4.33	4.17	4.26	4.13	4.21	4.08	4.19	4.06	4.14	4.00
H–C(5′)	4.85	4.57	4.85	4.56	4.85	4.55	4.87	4.54	4.87	4.55	4.89	4.55
HO–C(5′)	7.65	7.75	7.51	7.73	7.32	7.57	7.16	7.30	7.12	7.21	7.02	6.90
HO–C(2′)	[b])	[b])	5.22	5.31	[b])	[b])	[b])	[b])	[b])	[b])	5.47	5.52
HO–C(3′)	[b])	[b])	5.15	5.20	[b])	[b])	[b])	[b])	[b])	[b])	5.39	5.38
J(1′,2′)	7.2	8.1	7.5	8.1	7.5	7.8	7.5	7.8	7.8	7.8	7.8	7.5
J(2′,3′)	[b])	5.3	5.5	5.6	5.3	5.5	5.2	5.2	5.0	5.6	5.4	5.3
J(3′,4′)	[b])	[b])	1.0 [c])	1.0 [c])	1.2	1.0 [c])	1.5 [c])	1.2 [c])	1.2 [c])	1.2 [c])	1.0	1.2
J(4′,5′)	2.0	1.9	2.0	1.9	2.8	2.2	3.1	2.5	3.4	2.8	4.3	3.4
J(5′,OH)	[b])	[b])	2.2	1.5	3.4	1.9	4.4	2.5	4.4	2.5	4.7	3.1
J(2′,OH)	[b])	[b])	6.5	7.2	[b])	[b])	[b])	[b])	[b])	[b])	6.5	6.5
J(3′,OH)	[b])	[b])	3.7	3.5	[b])	[b])	[b])	[b])	[b])	[b])	3.2	3.1

[a]) Assignments may be interchanged, [b]) Not determined, [c]) The peak width at half height was taken.

The H–C(1′) *d* at 5.95 ppm couples with the H–C(2′) *ddd* at 4.75 ppm ($J = 7.8$, 6.5, and 5.4 Hz). Similarly, the H–C(1′) *d* at 5.96 ppm couples with the H–C(2′) *ddd* at 4.91 ppm ($J = 7.5$, 6.5, and 5.2 Hz). The DQFCOSY spectrum allowed to divide the signals into two sets, each one corresponding to a unit of the dimer. At this stage, the signals of **7** could not be assigned to a specific unit, while the assignment of the H–C(5′) signals of **8** (the desilylated analogue of **7**) to unit I or II is unambiguous, considering that only the H–C(5′) signal (*ddd*) at 4.55 ppm but not that at 4.89 ppm (br. *t*) shows a propargylic coupling (2.5 Hz). The assignment of the two sets of signals to the individual units of **7** is based on the expectation that the relative chemical-shift values will not be affected by desilylation. The small chemical-shift differences for **7** and **8** ($\Delta\delta \leq 0.03$ ppm) are in agreement with this expectation. The assignment of the br. *t* at 4.89 ppm ($J(5',OH) = 4.7$, $J(4',5') = 4.3$ Hz) to H–C(5′/I) of **7** and of the br. *t* at 4.55 ppm ($J(4',5') = 3.4$, $J(5',OH) = 3.1$ Hz) to H–C(5′/II), and the analogous assignment of their coupling partners is corroborated by the ROESY spectra of **7** (see below). The shift to lower fields for H–C(5′/I) correlates with the electron-acceptor effect of the C(7′) adenosyl substituent (*c.f.* [25]). This identification of the H–C(5′) signals allowed an unambiguous assignment of all CH and OH signals of the individual D-allofuranosyl units of **7**.

In the ROESY spectrum of **7** in (D_6)DMSO (*Table 2*), one finds cross-peaks between the HO–C(5′/I) *d* at 7.02 ppm and the *s*'s at 8.16 and 8.34 ppm, and similarly between HO–C(5′/II) (6.90 ppm) and the *s* at 8.13 ppm. One also finds cross-peaks between the *s* at 8.34 ppm and the H–C(1′/I) *d* (5.95 ppm), the H–C(2′/I) *ddd* (4.75 ppm), and the H–C(3′/I) *ddd* (4.33 ppm), and finally cross-peaks between the H–C(1′/II) *d* at 5.96 ppm and both the H–C(4′/I) *dd* (4.14 ppm) and the H–C(3′/I) *ddd* (4.33 ppm).

The cross-peak between HO–C(5′/II) and the *s* at 8.13 ppm allows to assign this *s* to H–C(2/II). Similarly, the cross-peaks of HO–C(5′/I) and those of the *s* at 8.34 ppm show that the *s*'s at 8.16 and 8.34 ppm correspond to H–C(2/I) and H–C(8/I), respectively. The cross-peaks between H–C(8/I), and H–C(1′/I) (5.95 ppm), H–C(2′/I) (4.75 ppm), and H–C(3′/I) (4.33 ppm) confirm the assignment of the two sets of signals to units I and II, respectively. The interaction between HO–C(5′/I) and both H–C(2/I) and H–C(8/I) evidences the *syn* and *anti* conformation for unit I of **7**, in keeping with the interactions of H–C(8/I) with H–C(1′/I), H–C(2′/I), and H–C(3′/I).

The evidence for both the *syn* and the *anti* conformations raises the question about their relative populations. The integrals of the cross-peaks correlate with the distance between HO–C(5′) and H–C(2) or H–C(8), and with the population of the *syn*/*anti* conformations. These H···H distances depend also on the conformation of the furanose ring and on the orientation of the *C*(4′)-substituent. A comparison of the $J(1',2')/J(3',4')$ ratios [29–32] for the solutions of **7** in (D_6)DMSO (7.8 (unit I) and 6.2 (unit II)) and in 28% (D_6)DMSO in $CDCl_3$ (7.5 (unit I) and 8.1 (unit II)) evidences that both ribosyl rings of **7** prefer the 2′-*endo* (*S*) conformation. It also suggests that this preference shows different solvent dependences for the two units, the 2′-*endo* conformation of unit I being more strongly favoured in (D_6)DMSO than in 28% (D_6)DMSO in $CDCl_3$, while the 2′-*endo* conformation for unit II appears to be more favoured for solutions in 28% (D_6)DMSO in $CDCl_3$ than in (D_6)DMSO.

Table 2. *Cross-Peaks in the ROESY Spectrum of* **7** *in 30% (D_6)DMSO in $CDCl_3$ and in (D_6)DMSO, and the Integrals of Some Selected Cross-Peaks*

Unit I	ROE with	
H–C(1′)	H–C(4′/I), H–C(3′/I), H–C(2′/I), H–C(8/I)	
H–C(2′)	H–C(1′/I), HO–C(5′/I), H–C(8/I)	
H–C(3′)	H–C(5′/I), HO–C(5′/I), H–C(8/I), H–C(1′/I), H–C(1′/II)	
H–C(4′)	H–C(5′/I), H–C(1′/I), H–C(1′/II), HO–C(5′/I)	
H–C(5′)	H–C(4′/I), H–C(3′/I), H–C(2′/I), HO–C(5′/I), H–C(8/I)	
HO–C(5′)	H–C(4′/I), H–C(3′/I), H–C(2′/I), H–C(8/I), H–C(5′/I), H–C(2/I)	
H–C(8)	H–C(3′/I), H–C(2′/I), H–C(1′/I), HO–C(5′/I), H–C(5′/I)	
H–C(2)	HO–C(5′/I)	
HO–C(2′) [a]	H–C(3′/I), H–C(2′/I), H–C(1′/I)	
HO–C(3′) [a]	H–C(4′/I), H–C(3′/I), H–C(2′/I), H–C(1′/I), H–C(1′/II)	
Unit II	**ROE with**	
H–C(1′)	H–C(4′/II), H–C(4′/I), H–C(3′/II), H–C(3′/I), H–C(2′/II)	
H–C(5′)	HO–C(5′/II)	
H–C(2′)	H–C(1′/II), HO–C(5′/II)	
H–C(3′)	HO–C(5′/II), H–C(1′/II)	
H–C(4′)	H–C(1′/II), HO–C(5′/II)	
HO–C(5′)	H–C(4′/II), H–C(3′/II), H–C(2′/II), H–C(5′/II), H–C(2/II)	
H–C(2)	HO–C(5′/II)	
HO–C(2′)	H–C(3′/II), H–C(3′/I), H–C(2′/II), H–C(1′/II)	
HO–C(3′) [a]	H–C(4′/II), H–C(3′/II), H–C(2′/II), H–C(1′/II)	
Cross-peaks	**ROE (integral of the cross-peaks)**	
	(D_6)DMSO in $CDCl_3$ (3 : 7)	(D_6)DMSO
H–C(2/I) with HO–C(5′/I)	15.7	9.6
H–C(8/I) with HO–C(5′/I)	6.6	12.1
H–C(2/II) with HO–C(5′/II)	29.7	24.6
H–C(8/I) with H–C(1′/I)	112.2	124.4
H–C(8/I) with H–C(2′/I)	19.3	65.0
H–C(8/I) with H–C(3′/I)	9.8	11.8

[a]) The cross-peaks for HO–C(2′/I) and HO–C(3′/II) overlap in 30% (D_6)DMSO in $CDCl_3$ and the cross-peaks for HO–C(3′/I) and HO–C(3′/II) overlap in (D_6)DMSO.

The relevant distances between HO–C(5′/I) and either H–C(2/I) or H–C(8/I) were estimated with the help of molecular modeling (*Macromodel*, Amber* force-field, gas phase). For this, we subjected a model in a 2′-*endo* conformation deduced from the coupling constants to energy minimisation, and checked for local minima by rotation about the C(4′)–C(5′), C(5′)–O(5′), and C(1′)–N(9) bonds. This led to a distance of 2.83 Å between HO–C(5′/I) and H–C(2/I), and 1.85 Å between HO–C(5′/I) and H–C(8/I) for the energetically preferred *gg* conformer. For a 1:1 *syn* ⇌ *anti* equilibrium (all else being equal), one thus expects a larger integral for the cross-peak between HO–C(5′/I) and H–C(8/I) than for the cross-peak between HO–C(5′/I) and H–C(2/I).

The integrals (*Table 2*)[3]) for the cross-peaks of **7** in 30% (D_6)DMSO in $CDCl_3$ are 6.6 for HO–C(5′/I)/H–C(8/I) and 15.7 for HO–C(5′/I)/H–C(2/I). Other integrals

[3]) Lack of an appropriate reference cross-peak prevented volume integration.

are 112.2 for H–C(1′/I)/H–C(8/I), 19.3 for H–C(2′/I)/H–C(8/I), and 9.8 for H–C(3′/I)/H–C(8/I); the integral is 29.7 for HO–C(5′/II)/H–C(2/II). These values evidence a higher population of the *syn* conformer, and a higher population of the *syn* conformer in unit II than in unit I. The larger integral for the H–C(1′/I)/H–C(8/I) cross-peak than for the cross-peak of H–C(8/I) with H–C(2′/I) and H–C(3′/I) confirms that unit I adopts preferentially the *syn* conformation [33].

Assuming that the *syn* conformation is correlated with an intramolecular C(5′)–OH···N(3) H-bond that is expected to be at least partially disrupted in (D_6)DMSO [27][28], we also measured the integrals of the cross-peaks for **7** in this solvent. The expected shift of the *syn* ⇌ *anti* equilibrium for **7** upon changing the solvent from 30% (D_6)DMSO in $CDCl_3$ to (D_6)DMSO is evidenced by the change of the integrals for the cross-peaks HO–C(5′/I)/H–C(8/I) (6.6 → 12.1) and HO–C(5′/I)/H–C(2/I) (15.7 → 9.6). For solutions of **7** in (D_6)DMSO, an increase of the integrals for the H–C(1′/I)/H–C(8/I) (112.2 → 124.4) and H–C(2′/I)/H–C(8/I) (19.3 → 65.0) cross-peaks evidences a change in the preferred orientation of the base moiety about the glycosidic bond, shortening the average distance between H–C(8/I) and H–C(1′/I) and, particularly, between H–C(8/I) and H–C(2′/I). That the integral for the H–C(8/I)/H–C(1′/I) (124.4) is larger than that for the H–C(8/I)/H–C(2′/I) (65.0) cross-peak suggests that the *syn* conformation for unit I is (still) preferred for solutions of **7** in (D_6)DMSO [33], but much less so than for solutions in 30% (D_6)DMSO in $CDCl_3$.

The small difference between the integrals for the HO–C(5′/II)/H–C(2/II) cross-peak (29.7 → 24.6) in the two solvents evidences that unit II adopts predominantly the *syn* conformation even in (D_6)DMSO.

To characterize the intramolecular C(5′/I)–OH···N(3) H-bond, we analysed the J(H,OH), δ(OH), and $\Delta\delta/\Delta T$ values. There is ample evidence that a comparison of these parameters for ^{1}H-NMR spectra of alcohols in $CDCl_3$ and in (D_6)DMSO allows characterisation of intramolecular H-bonds [27][28].

The J(5′,OH) values for **7** in (D_6)DMSO and in mixtures of $CDCl_3$ and (D_6)DMSO are listed in *Tables 1* and *3*. Their interpretation requires information about the J(H,OH) value for a freely rotating OH group of an aliphatic propargylic alcohol, and about the J(H,OH) value for a HO–C(5′) group of an appropriate model compound with a completely persistent intramolecular H-bond to N(3). The former value is J(H,OH) = 5.6 Hz for **9**, while **10** and **11** were taken as model compounds for purine nucleosides with a persistent intramolecular C(5′)–OH···N(3) H-bond in $CDCl_3$ [24]. The *C*(8)-unsubstituted **10** (J(5′,OH) = 1.5 Hz) was expected to be a suitable model compound for unit I of **7**, and the *C*(8)-Cl-substituted **11** (J(5′,OH) = 0.5 Hz) [34] was similarly expected to be a suitable model for unit II of **7**, leading to two scales for the J(H,OH) values, one ranging from 1.5 to 5.6 Hz and the other one ranging from 0.5 to 5.6 Hz, corresponding to 100% and 0% persistence of the H-bond, respectively. The persistencies of the C(5′)–OH···N(3) H-bonds derived by interpreting J(5′,OH) according to these scales are shown in *Table 3*. To check for the consistency of these values, we correlated them with the conformation about the C(4′)–C(5′) bonds of **7**, as expressed by J(4′,5′). For this, we calculated J(4′,5′) by taking into account the population of the *gg* conformers corresponding to the persistency of C(5′)–OH···N(3) H-bonds as deduced from J(5′,OH) and the population of the conformations of the non-H-bonded tautomers. These tautomers were assumed to adopt a 1:1:1 equilibrium

of the freely rotating *gg/gt/tg* conformers[4] ($J(gg) = 2.1$, $J(gt) = 2.1$ and $J(tg) = 9.3$ Hz)[5]. The values for $J(4',5')$ correlating with the C(5′)–OH···N(3) H-bond were taken from the ^{1}H-NMR spectra of **10** (1.5 Hz) and **11** (2.0 Hz). The difference between these values evidences the influence of the C(8)–Cl substituent on the conformation of the H-bonded tautomer of these nucleosides.

Table 3. *Persistency of H-Bonds in* **7**, *as Deduced from* J(*H–C(5′, OH)*. Correlation of the persistency with the C(4′)–C(5′) *gg* conformation (*c.f.* text for the calculation of $J(4',5')$).

With **10** *as model compound*

(D_6)DMSO in $CDCl_3$ [%]	Persistency [%]		$J(5'/,OH/I)$	$J(5',OH/II)$	$J(4',5'/I)$			$J(4',5'/II)$	
	Unit I	Unit II			Observed	Calculated [a])	Calculated [b])	Observed	Calculated
28	*83*	100	2.2	1.5	2.0	2.0	2.1	1.9	1.5
40	*54*	90	3.4	1.9	2.8	2.9	3.1	2.2	1.8
60	*30*	76	4.4	2.5	3.1	3.5	4.1	2.5	2.2
80	*30*	76	4.4	2.5	3.4	3.5	4.1	2.8	2.2
100	*22*	61	4.7	3.1	4.3	3.8	4.3	3.4	2.6

With **11** *as model compound*

(D_6)DMSO in $CDCl_3$ [%]	Persistency [%]		$J(5'/,OH/I)$	$J(5',OH/II)$	$J(4',5'/I)$		$J(4',5'/II)$		
	Unit I	Unit II			Observed	Calculated	Observed	Calculated [c])	Calculated [b])
28	67	*80*	2.2	1.5	2.0	2.9	1.9	2.6	2.2
40	43	*72*	3.4	1.9	2.8	3.4	2.2	2.7	2.5
60	24	*61*	4.4	2.5	3.1	3.8	2.5	3.0	2.9
80	24	*61*	4.4	2.5	3.4	3.8	2.8	3.0	2.9
100	18	*50*	4.7	3.1	4.3	4.0	3.4	3.3	3.3

[a]) Calculated with $J(4',5') = 1.5$ Hz for the H-bonded tautomer and a 1 : 1 : 1 ratio (*gg*/*gt*/*tg*) of the rotamers. [b]) Calculated with $J(4',5') = 1.5$ Hz for the H-bonded tautomer and a 1 : 1 : 1.4 ratio (*gg*/*gt*/*tg*) of the rotamers. [c]) Calculated with $J(4',5') = 2.0$ Hz for the H-bonded tautomer and a 1 : 1 : 1 ratio (*gg*/*gt*/*tg*) of the rotamers.

The results of these calculations are listed in *Table* 3. As expected, use of **10** as model compound leads to a smaller difference between the experimental and calculated $J(4',5')$ values for unit I; similarly, use of **11** as model compound leads to a better correspondence between the experimental and calculated $J(4',5')$ values for unit II of **7**. This evidences that the combination of the persistencies for units I and II indicated in italics in *Table 3* is more reliable than values derived from using a single model compound. The correspondence between experimental and calculated $J(4',5')$ values for unit I (with **10** as model compound) is better for solutions in the less polar solvent mixtures, while the correspondence for unit II is better for solutions in (D_6)DMSO. That $J(4',5')$ (obs.) for unit I of **7** in (D_6)DMSO is larger than $J(4',5')$ (calc.) suggests that the assumption of an equidistribution of rotamers for the non-H-bonded tautomer of **7** has to be corrected in favour of a larger proportion of the *tg* rotamer. Assuming a *gg/gt/tg* ratio of 1 : 1 : 1.4 results in a much smaller difference between $J(4',5')$ (obs.) and $J(4',5')$ (calc.) for solutions in (D_6)DMSO, a good

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[4]) While the *gg* and *gt* conformers are preferred over the *tg* conformers in the natural nucleosides, introduction of the ethynyl substituent (D-*allo*-isomer) leads to the destabilization of the *gg* and *gt* conformers by electronic (loss of stabilizing *gauche* interaction) and steric effects.

[5]) Using the extended *Karplus* equation of *Altona* and *Sundaralingam* [31][32][35] as implemented in the Macromodel V 6.0 programme.

correspondence of these values for 28% (D_6)DMSO in $CDCl_3$, but a worse correlation for the intermediate solvent mixtures. An increasingly higher proportion of the *tg* rotamers is also evidenced by the $J(4',5')$ value for analogues of **10** and **11** possessing an increasingly bulkier substituent at C(8) [24][25]. The coincidence of the observed and calculated values for **7** in 28% (D_6)DMSO in $CDCl_3$ reflects the appropriate choice of **10** as model. The choice of **11**, which possesses a Cl instead of an alkynyl substituent at C(8), as model compound for unit II is less fortunate, as suggested by the difference between observed and calculated values for **7** in 28% (D_6)DMSO in $CDCl_3$. A better, if not fully satisfactory, coincidence between observed and calculated values for $J(4',5')$ results by assuming $J(4',5') = 1.5$ Hz for the H-bonded tautomer also of unit II, and a similar distribution of rotamers as for unit I. Thus, the comparison of $J(5',OH)$ and $J(4',5')$ values indicates that **10** is an appropriate model for unit I, that $J(5',OH)$ is a valid parameter for the persistency of the intramolecular H-bond in this unit, and that the *tg* rotamer is favoured. It is not possible to deduce to what extent the difference between the observed and calculated $J(4',5')$ values for unit II of **7** is due to an underestimation of the persistency of the intramolecular H-bond and/or the preference of the *tg* rotamer. The Cl substituent at C(8) of **11** and the alkynyl substituent at C(8) of **7** lead to slightly different conformations of the H-bonded tautomers.

This interpretation agrees qualitatively with the solvent dependence of the chemical shift (*Tables 1* and *4*). Remarkably, the largest change of the chemical shift for HO–C(5′) of the two units upon increasing the concentration of (D_6)DMSO is for the change from 28 to 40% for unit I, and from 80% to pure (D_6)DMSO for unit II, in agreement with the more persistent C(5′)–OH···N(3) H-bond in unit II[6]).

Table 4. *Difference of the Chemical Shift Values* [ppm] *of HO–C(5′) of Units I and II of* **7** *for Solutions in (D_6)DMSO and in $CDCl_3$ with Increasing Amounts of (D_6)DMSO and Correlation between the Change in the Chemical Shifts* [ppm] *of HO–C(5′) upon Increasing the Amount of (D_6)DMSO in $CDCl_3$*

(D_6)DMSO in $CDCl_3$ [%]	Chemical shift of HO–C(5′)		$\Delta^1\delta$ [a])	$\Delta^2\delta$ [b])	
	Unit I	Unit II		Unit I	Unit II
21	7.65	7.75	0.1		
28	7.51	7.73	0.22	0.14	0.02
40	7.32	7.57	0.25	0.19	0.16
60	7.16	7.30	0.14	0.16	0.27
80	7.12	7.21	0.09	0.04	0.09
100	7.02	6.90	−0.12	0.10	0.31

[a]) $\Delta^1\delta = \delta(HO–C(5'/II)) – \delta(HO–C(5'/I))$. [b]) $\Delta^2\delta$ = Change in the chemical shift upon increasing the amount of (D_6)DMSO in $CDCl_3$.

The $\Delta\delta/\Delta T$ values for the two HO–C(5′) of **7** were determined for solutions in pure (D_6)DMSO and in 28% (D_6)DMSO in $CDCl_3$ and (*Table 5*). A reference value for fully solvated propargylic alcohols was obtained from $\Delta\delta/\Delta T$ for HO–C(3) of **9** [26] in the same solvents (*Table 5*). The $\Delta\delta/\Delta T$ values for HO–C(3) of **9** and for

[6]) The difference between the chemical shifts (*Table 4*) for HO–C(5′) of these units is maximal at a concentration of 40% (D_6)DMSO in $CDCl_3$; this appears to be the concentration of (D_6)DMSO that induces the largest difference in the persistency of intramolecular H-bonds of these OH groups.

HO–C(5′), HO–C(3′), and to a lesser extent also HO–C(2′) of **7** in (D_6)DMSO, are similar (*Table 5*), implying that HO–C(5′) is mostly solvated in (D_6)DMSO. This is at variance with the results discussed above, suggesting that $\Delta\delta/\Delta T$ values are a more complex parameter of intramolecular H-bonds than coupling constants and chemical-shift values. The $\Delta\delta/\Delta T$ value for HO–C(3) of **9** in 28% (D_6)DMSO in $CDCl_3$ is 10.9 ppb/K, while $\Delta\delta/\Delta T$ values for HO–C(3′) and HO–C(2′) in this solvent mixture are smaller (5.1 to 7.7, resp.); intermediate values characterize $\Delta\delta/\Delta T$ for HO–C(5′) in this solvent mixture (8.8 ppb/K for unit I and 7.6 for unit II). This means that the large $\Delta\delta/\Delta T$ for **9** reflects the solvent effect on a propargylic OH group, while the $\Delta\delta/\Delta T$ values for HO–C(5′) evidence partially persistent C(5′)–OH···N(3) H-bonds for **7** in this solvent mixture. Again, a higher persistency is deduced for the H-bond in unit II than in unit I.

Table 5. *$\Delta\delta/\Delta$T Values* [ppb/K] *for HO–C(5′), HO–C(2′) and HO–C(3′) of* **7** *and HO–C(3) of* **9** *in $CDCl_3$, (D_6)DMSO, and in a Mixture of 28% of (D_6)DMSO in $CDCl_3$*

(D_6)DMSO in $CDCl_3$ [%]	$\Delta\delta/\Delta T$ Values						
	7						**9**
	HO–C(5′/I)	HO–C(5′/II)	HO–C(2′/I)	HO–C(2′/II)	HO–C(3′/I)	HO–C(3′/II)	HO–C(3)
0	–	–	–	–	–	–	2.5
28	8.8	7.6	5.1	5.5	6.4	7.7	10.9
100	6.0	5.6	4.8	5.2	5.4	5.6	5.7

Force-field calculations (*Macromodel,* Amber*, gas phase) for unit I of the dimer **8**, starting with a structure possessing a C(5′/I)–OH···N(3) H-bond, a *2′-endo* conformation and a H–C(5′/I)–C(4′/I)–H dihedral angle of 62° (corresponding to $J(4',5') = 2.1$ Hz), constraining unit II suggest a χ angle of *ca.* 50° for unit I, corresponding to a *syn* conformation.

These observations and interpretations show that the *syn* conformation is strongly preferred for **7**, particularly for unit II that is relevant to the oligonucleotides of type **2**. They lead to an unfavourable prediction for the pairing abilities of these analogues.

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Experimental Part

General. Solvents were distilled before use: THF from K/benzophenone, CH_2Cl_2 from CaH_2. Reactions were run under Ar. Qual. TLC: precoated silica-gel plates (*Merck* silica gel *60 F_{254}*); detection by spraying with 'mostain' (400 ml of 10% aq. H_2SO_4, 20 g of $(NH_4)_6Mo_7O_{24}\cdot H_2O$, 0.4 g of $Ce(SO_4)_2$) and heating. Flash chromatography (FC): silica gel *Merck 60* (0.04–0.063 mm). Optical rotations: 1-dm cell at 25° and 589 nm. FT-IR: 1–2% soln. in the indicated solvent. ^{1}H- and ^{13}C-NMR: at 200, 300, 400, or 500 MHz, and 50, 75, 100, or 125 MHz, resp. MS: matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF; indol-3-acrylic-acid (IAA), 0.05M in THF or α-cyano-4-hydroxycinnamic acid (CCA) 0.05M in MeCN/EtOH/H_2O and 2,5-dihydroybenzoic acid (DHB) 0.05M in THF for high-resolution (HR) MALDI-MS.

*9-[6,7-Dideoxy-2,3-*O*-isopropylidene-7-*C*-(trimethylsily)-β-*D*-allo-hept-6-ynofuranosyl]-8-iodoadenine* (**4**). At −78°, a soln. of (i-Pr)$_2$NH (2.5 ml, 18 mmol, distilled from CaH_2) in THF (20 ml) was treated dropwise with 1.6M BuLi in hexane (11.2 ml, 18 mmol), stirred for 15 min, warmed to 0° for 15 min, cooled to −78°, treated dropwise with a soln. of **3** (1.3 g, 2.5 mmol) in THF (15 ml), stirred for 2.5 h, treated dropwise with a soln. of *N*-iodosuccinimide (NIS; 3.1 g, 14 mmol) in THF (15 ml), stirred for 1.5 h, treated with sat. NH_4Cl soln. (10 ml),

and allowed to warm to 23°. After evaporation, a soln. of residue in AcOEt was washed with cold sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. After filtration through a short pad of silica gel (hexane /AcOEt 1:1) and evaporation, a soln. of the residue in THF (20 ml) was treated with 8M $MeNH_2$ soln. (1.75 ml, 14 mmol) in THF (20 ml), stirred for 2 h, and evaporated. A soln. of the residue in AcOEt was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (hexane/AcOEt 1:1) gave **4** (1.042 g, 75%). Off-white solid. M.p. 162° (dec.). R_f ($CHCl_3$/MeOH 95:5) 0.37. $[\alpha]_D^{25} = -122.4$ ($c = 1$, $CHCl_3$). UV ($CHCl_3$): 266 (24000). IR ($CHCl_3$): 3522*w*, 3473*w*, 3410*w*, 3169*w*, 3007*w*, 2180*w*, 1634*s*, 1597*w*, 1580*m*, 1528*w*, 1485*w*, 1445*w*, 1419*w*, 1368*w*, 1318*w*, 1285*m*, 1267*m*, 1252*m*, 1154*w*, 1093*m*, 1045*w*, 1003*w*, 970*w*, 959*w*, 908*w*, 849*m*. ^{1}H-NMR (300 MHz, $CHCl_3$): 8.17 (*s*, H–C(2)); 7.65 (*s*, HO–C(5′)); 6.00 (*d*, $J = 5.4$, H–C(1′)); 5.95 (br. *s*, NH_2); 5.21 (*t*, $J = 5.4$, H–C(2′)); 5.14 (*dd*, $J = 5.4, 1.0$, H–C(3′)); 4.70 (*t*, $J \approx 1.7$, H–C(4′)); 4.53 (*d*, $J = 1.7$, H–C(5′)); 1.71, 1.42 (2*s*, Me_2C); 0.20 (*s*, Me_3Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.95 (*s*, C(6)); 152.48 (*d*, C(2)); 149.65 (*s*, C(4)); 123.62 (*s*, C(5)); 114.25 (*s*, Me_2C); 101.75 (*d*, C(8)); 99.51 (*s*, C(6′)); 96.18 (*d*, C(1′)); 91.99 (*s*, C(7′)); 87.27 (*d*, C(4′)); 81.86 (*d*, C(2′)); 80.88 (*d*, C(3′)); 63.71 (*d*, C(5′)); 27.84, 25.55 (2*q*, Me_2C); –0.22 (*q*, Me_3Si). HR-MALDI-MS: 530.0718 ($[M^+ + H]^+$; calc. 530.0721).

*9-(6,7-Dideoxy-2,3-*O*-isopropylidene-β-*D*-*allo*-hept-6-ynofuranosyl)adenine* (**5**). At 25°, a soln. of **3** (1.2 g, 2.3 mmol) in THF (20 ml) was treated with 8M $MeNH_2$ in THF (2.3 ml, 19 mmol), stirred for 2 h, and evaporated. A soln. of the residue in THF (20 ml) was treated with 1M Bu_4NF in THF (2.8 ml, 2.8 mmol), stirred for 2 h, and evaporated. A soln. of the residue in AcOEt (100 ml) was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane/MeOH 10:9:1) gave **5** (0.55 g, 70%). White solid. M.p. 210° (dec). R_f ($CHCl_3$/MeOH 95:5) 0.27. R_f (AcOEt/hexane/MeOH 10:9:1) 0.22. $[\alpha]_D^{25} = -136.7$ ($c = 0.525$, $CHCl_3$/MeOH 3:2). UV ($CHCl_3$/MeOH 3:2): 260 (14628). IR (KBr): 3288*s*, 3134*s*, 1676*s*, 1608*s*, 1576*m*, 1512*w*, 1474*m*, 1423*m*, 1381*m*, 1341*m*, 1301*m*, 1283*w*, 1264*m*, 1222*m*, 1155*w*, 1103*m*, 1082*m*, 1068*m*, 991*m*, 967*w*, 938*w*, 909*w*, 856*w*, 798*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 8.24 (*s*, H–C(8)); 8.15 (*s*, H–C(2)); 7.32 (br. *s*, NH_2); 6.26 (*d*, $J = 5.3$, HO–C(5′)); 6.12 (*d*, $J = 3.1$, H–C(1′)); 5.26 (*dd*, $J = 3.1, 5.9$, H–C(2′)); 5.04 (*dd*, $J = 6.2, 1.9$, H–C(3′)); 4.39 (*dd*, $J = 5.3, 2.2$, H–C(5′)); 4.16 (*dd*, $J = 1.8, 5.3$, H–C(4′)); 3.28 (*d*, $J = 2.2$, H–C(7′)); 1.25, 1.37 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.38 (*s*, C(6)); 152.85 (*d*, C(2)); 148.95 (*s*, C(4)); 139.79 (*d*, C(8)); 119.12 (*s*, C(5)); 113.26 (*s*, Me_2C); 90.12 (*d*, C(1′)); 88.18 (*d*, C(4′)); 83.23 (*d*, C(2′)); 82.94 (*s*, C(6′)); 81.11 (*d*, C(3′)); 76.39 (*s*, C(7′)); 61.29 (*d*, C(5′)); 26.97, 25.09 (2*q*, Me_2C). HR-MALDI-MS: 332.1355 ($[M + H]^+$; calc. 332.1359).

*9-[6,7-Dideoxy-2,3-*O*-isopropylidene-7-*C*-(trimethylsilyl)-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* (**6**). A soln. of **5** (0.15 g, 0.45 mmol), **4** (0.31 g, 0.59 mmol), [Pd_2(dba)$_3$] (16.2 mg, 0.018 mmol), CuI (8.6 mg, 0.045 mmol), and P(fur)$_3$ (6.2 mg, 0.027 mmol) in degassed Et_3N/toluene 1:1 (5 ml) was stirred for 18 h at 23°. Evaporation and FC ($CHCl_3$/MeOH 95:5) gave **6** (0.288 g, 86%). Yellowish brown solid. M.p. 180° (dec) . R_f ($CHCl_3$/MeOH 95:5) 0.2. $[\alpha]_D^{25} = -106.8$ ($c = 1$, $CHCl_3$/MeOH 3:2). UV ($CHCl_3$/MeOH 3:2): 266 (12487), 245 (19483). IR (KBr): 3333*m*, 3188*m*, 2988*m*, 1650*m*, 1600*m*, 1577*m*, 1479*w*, 1418*w*, 1376*m*, 1330*m*, 1302*m*, 1250*m*, 1216*m*, 1156*w*, 1089*m*, 970*w*, 850*m*, 798*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 8.33 (*s*, H–C(8/I)); 8.16 (*s*, H–C(2/I), H–C(2/II)); 7.66 (br. *s*, NH_2); 7.37 (br. *s*, NH_2); 6.68 (*d*, $J = 5.8$, HO–C(5′/I)); 6.36 (*d*, $J = 5.2$, HO–C(5′/II)); 6.24 (*d*, $J = 2.7$, H–C(1′/I)); 6.12 (*d*, $J = 3.2$, irrad. at 5.45 → *s*, H–C(1′/II)); 5.45 (*dd*, $J = 3.2, 6.2$, irrad. at 5.09 → *d*, $J = 3.2$, H–C(2′/II)); 5.41 (*dd*, $J = 2.7, 5.9$, H–C(2′/I)); 5.20 (*dd*, $J = 6.0, 2.5$, H–C(3′/I)); 5.09 (*dd*, $J = 6.0, 2.3$, irrad. at 4.08 → *d*, $J = 6.0$, H–C(3′/II)); 4.84 (*t*, $J = 6.0$, H–C(5′/I)); 4.42 (*dd*, $J = 5.3, 6.6$, H–C(5′/II)); 4.30 (*dd*, $J = 2.1, 6.2$, irrad. at 4.84 → *d*, $J = 2.1$, H–C(4′/I)); 4.08 (*dd*, $J = 2.2, 6.7$, irrad. at 4.42 → *d*, $J = 2.2$, H–C(4′/II)); 1.57, 1.50, 1.36, 1.30 (4*s*, 2 Me_2C); 0.07 (*s*, Me_3Si). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.41, 156.35 (2*s*, C(6/I), C(6/II)); 153.85, 152.90 (2*d*, C(2/I), C(2/II)); 148.87, 148.14 (2*s*, C(4/I) C(4/II)); 140.02 (*d*, C(8/I)); 132.37 (*s*, C(8/II)); 119.18, 119.05 (2*s*, C(5/I), C(5/II)); 113.47, 113.36 (2*s*, 2 Me_2C); 105.51 (*s*, C(6′/II)); 95.27 (*s*, C(6′/I)); 90.45, 89.88 (2*d*, C(1′/I), C(1′/II)); 89.20 (*s*, C(7′/II)); 87.98, 87.94 (2*d*, C(4′/I), C(4′/II)); 83.38, 82.00 (2*d*, C(2′/I), C(2′/II)); 81.68, 81.40 (2*d*, C(3′/I), C(3′/II)); 73.55 (*s*, C(7′/I)); 61.87, 61.81 (2*d*, C(5′/I), C(5′/II)); 26.94, 25.11 (2*q*, Me_2C); 25.16 (2*q*, Me_2C); –0.34 (*q*, Me_3Si). HR-MALDI-MS: 755.2747 ($[M^+ + Na]$; calc. 755.2698).

*9-[6,7-Dideoxy-7-*C*-(trimethylsily)-β-*D*-allo-hept-6-ynofuranosyl]adenin-8-yl-(8 → 7′)-9-(6,7-dideoxy-β-*D*-al lo-hept-6-ynofuranosyl)adenine* (**7**). A soln. of CF_3COOH (2.5 ml) in H_2O (5 ml) was treated at 25° with a soln. of **6** (0.1 g, 0.14 mmol) in THF (12 ml), stirred for 10 min, and evaporated. The suspension of the residue in THF (1 ml) was treated with 8M $MeNH_2$ in THF (0.5 ml), stirred for 10 min, and evaporated. FC ($CHCl_3$/MeOH 86:14) gave **7** (0.0783 g, 88%).White solid. M.p. 180° (dec). R_f ($CHCl_3$/MeOH 85:15) 0.14. $[\alpha]_D^{25} = -20.4$ ($c =$ 0.51, DMSO). UV ($CHCl_3$/MeOH 3:2): 267 (8880), 300 (*sh*, 6921). IR (KBr): 3323*m*, 3201*m*, 2184*w*, 1652*m*, 1616*m*, 1479*w*, 1427*w*, 1377*w*, 1333*w*, 1250*w*, 1204*m*, 1131*m*, 1075*m*, 956*w*, 847*m*, 798*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 1*; additionally, 0.11 (*s*, Me_3Si). ^{13}C-NMR (75 MHz, (D_6)DMSO): 156.47, 156.43 (2*s*, C(6/II), C(6/I)); 153.30, 152.61 (2*d*, C(2/I), C(2/II)); 149.23, 148.05 (2*s*, C(4/I), C(4/II)); 140.13 (*d*, C(8/I)); 133.24 (*s*,

C(8/II)); 119.49 (2*s*, C(5/I), C(5/II)); 104.74 (*s*, C(6′/II)); 94.84 (*s*, C(6′/I)); 89.64, 88.74 (2*d*, C(1′/I), C(1′/II)); 89.24 (*s*, C(7′/II)); 87.83, 87.67 (2*d*, C(4′/I), C(4′/II)); 73.61 (*s*, C(7′/I)); 73.13, 71.82 (2*d*, C(2′/I), C(2′/II)); 70.60, 70.32 (2*d*, C(3′/I), C(3′/II)); 62.80, 62.74 (2*d*, C(5′/I), C(5′/II)); −0.30 (*q*, Me_3Si). HR-MALDI-MS: 675.2035 ($[M+Na]^+$; calc. 675.2072).

*9-(6,7-Dideoxy-β-*D*-allo-hept-6-ynofuranosyl)adenin-8-yl-(8 → 7′)-9-(6,7-dideoxy-β-*D*-allo-hept-6-ynofuranosyl)adenine* (**8**). A soln. of **7** (0.03 g, 0.046 mmol) in THF (10 ml) was treated with 1M $Bu_4NF \cdot 3\ H_2O$ in THF (0.05 ml, 0.055 mmol), stirred for 30 min, and evaporated. FC ($CHCl_3$/MeOH 85:16) gave **9** (0.014 g, 54%). White solid. R_f ($CHCl_3$/MeOH 7:3) 0.32. ^{1}H-NMR (500 MHz, (D_6)DMSO): 8.34 (*s*, H−C(8)); 8.16 (*s*, H−C(2/I)); 8.15 (*s*, H−C(2/II)); 7.76 (br. *s*, NH_2); 7.44 (br. *s*, NH_2); 7.04 (*d*, *J* = 4.8, HO−C(5′/I)); 6.85 (*d*, *J* = 3.3, HO−C(5′/II)); 5.97 (*d*, *J* = 8.0, H−C(1′/II)); 5.94 (*d*, *J* = 8.0, H−C(1′/I)); 5.54 (*d*, *J* = 6.8, HO−C(2′/II)); 5.50 (*d*, *J* = 6.8, HO−C(2′/I)); 5.44 (*d*, *J* = 3.8, HO−C(3′/I)); 5.42 (*d*, *J* = 4.0, HO−C(3′/II)); 4.94 (*ddd*, *J* = 8.0, 6.8, 5.0, H−C(2′/II)); 4.89 (br. *t*, *J* ≈ 4.6, H−C(5′/II)); 4.75 (*ddd*, *J* = 8.0, 6.8, 5.2, H−C(2′/I)); 4.55 (*ddd*, *J* = 4.5, 3.3, 2.5, H−C(5′/I)); 4.33 (*ddd*, *J* = 5.2, 3.8, 1.0, H−C(3′/I)); 4.28 (*ddd*, *J* = 5.0, 4.0, 1.0, H−C(3′/II)); 4.14 (*dd*, *J* = 4.5, 1.0, H−C(4′/I)); 4.02 (*dd*, *J* = 4.5, 1.0, H−C(4′/II)); 3.35 (*d*, *J* = 2.5, H−C(7′)). MALDI-MS: 581 ($[M+H]^+$), 603 ($[M+Na]^+$).

4-Methyl-1-(trimethylsilyl)pent-1-yn-3-ol (**9**). Prepared according to the procedure of *Kitano et al.* [26]. Distillation gave **9** (1.57 g, 87%). Colourless liquid. B.p. 75°/17 mbar, ([36]: 99°/30 Torr). ^{1}H-NMR (300 MHz, $CDCl_3$) : 4.15 (*t*, *J* = 5.6, H−C(3)); 1.87 (*oct.*, *J* = 5.1, H−C(4)); 1.76 (*d*, *J* = 5.6, HO−C(3)); 1.01, 0.99 (2*d*, *J* = 5.0, Me_2CH); 0.18 (*s*, Me_3Si). ^{1}H-NMR (300 MHz, (D_6)DMSO)) : 5.31 (*d*, *J* = 5.6, HO−C(3)); 3.96 (*t*, *J* = 5.6, H−C(3)); 1.68 (*oct.*, *J* = 5.1, H−C(4)); 0.90, 0.87 (2*d*, *J* = 5.0, Me_2CH); 0.13 (*s*, Me_3Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 105.75 (*s*, C(2)); 90.27 (*s*, C(1)); 68.43 (*d*, C(3)); 34.56 (*d*, C(4)); 18.22, 17.59 (2*q*, 2 Me); 0.04 (*s*, Me_3Si).

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