Oligonucleosides with a Nucleobase-Including Backbone

Part 11

Linear and Convergent Synthesis of Ethynylene-Linked Uridine-Derived Oligomers

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A linear and a convergent synthesis of uridine-derived backbone-base-dedifferentiated (backbone including) oligonucleotide analogues were compared. The *Sonogashira* cross-coupling of the alkyne **1** and the iodide **2** gave the dimer **4** that was *C*-desilylated and again coupled with **2** to give the trimer **6** (*Scheme 1*). Repeating this linear sequence led to the pentamer **10**. Coupling yields were satisfactory up to formation of the trimer **6**, but decreased for the coupling to higher oligomers. Similarly, coupling of the alkynes **5**, **7**, and **9** with the iodouridine **3** gave, in decreasing yields, the trimer **12**, tetramer **13**, and pentamer **14**, respectively. The dimeric iodouracil **20** was synthesized by coupling the alkyne **17** with the iodide **16** to the dimer **18**, followed by iodination at C(6/I) to **19** and *O*-silylation (*Scheme 2*). The iodinated dimer **23** was prepared by iodinating and *O*-silylating the known dimer **21**. Coupling of **20** and **23** with the dimer **5**, trimer **7**, and tetramer **9** gave the tetramers **8** and **13**, the pentamers **10** and **14**, and the hexamer **15**, respectively (*Scheme 3*). The oligomers up to the pentamer **14** were deprotected to provide the trimer **24**, tetramer **25**, and pentamer **26** (*Scheme 4*). There was no evidence for the heteropairing of the pentamer **26** and rA_7, nor for the pairing of rU_5 and rA_7, while a UV melting experiment showed the beginning of a sigmoid curve for the interaction of rU_7 with rA_7. Therefore, the pentamer **26** does not pair more strongly with rA_7 than rU_5.

Introduction. – In our quest for autonomously pairing oligonucleotide analogues that do not, strictly speaking, differentiate nucleobases from the backbone, we have so far designed three generations of analogues, *viz.* phosphodiester analogues of DNA oligomers, neutral, ethynylene-linked (=ethyne-1,2-diyl-linked) analogues of RNA oligomers, and ether-linked RNA oligomers. We reported the synthesis of protected phosphodiester-linked decamers, their partially successful deprotection, and the incorporation of corresponding deoxyribose- and deoxyerythrose-derived monomers into a DNA 14-mer [1–3]. The second generation of analogues is still under scrutiny. We have so far reported the synthesis of monomers and dimers required for the preparation of ethynylene-linked oligomers [4–6], the synthesis of a corresponding adenosine-derived tetramer [7], and the conformational analysis of an adenosine-derived dimer [8]. This analysis showed that the substitution at C(8) of adenosine in combination with the intramolecular H-bond of the propargylic HO–C(5′) to N(3) results in a very strong preference for the *syn*-conformation. As we had assumed, on the basis of indicative force-field calculations and model studies, that the autonomous pairing of these analogues required an *anti*-conformation, we designed a third generation of analogues that should pair in the *syn*-conformation. Partially protected, self-complementary ether-linked dimers indeed pair in $CHCl_3$ solution [9][10]. Independently of pursuing our studies of this type of analogues, we planned to

experimentally test the assumption that ethynylene-linked oligomers only pair in the *anti*-conformation; we also wished to learn if such oligomers pair with oligomeric RNA.

Uridine-derived oligomers **A** are required to test the pairing properties with the C(5′)–C(8) ethynylene-linked adenosine counterpart **B** (homopairing) and with RNA (heteropairing; *Fig. 1*). We planned to investigate a linear and a convergent approach to the synthesis of uridine-derived oligomers. The linear approach features a *Sonogashira* coupling of the mono- to pentameric alkynes **1**, **5**, **7**, and **9** with the 6-iodouridine **2**, followed by deprotection of the *C*-silylated coupling products (*cf. Scheme 1*). A final coupling with the monomer **3** should introduce a terminal unit that is devoid of a *C(5′)*-ethynyl group. In a shorter, convergent approach the iodinated dimers **20** and **23** should be coupled to the monomer **5**, trimer **7**, and tetramer **9** (*cf. Scheme 3*).

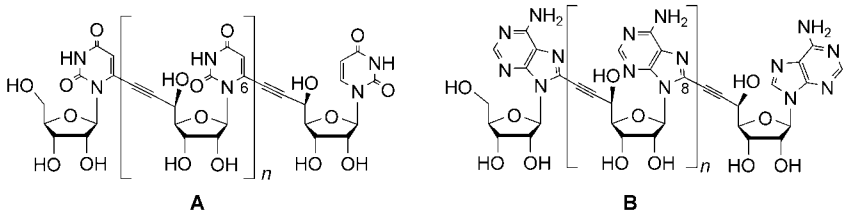

Fig. 1. *Uridine- and adenosine-derived ethynylene-linked oligonucleosides* **A** *and* **B**

Results and Discussion. – The first reaction cycle characterising the linear approach to the uridine-derived oligomers started with the *Sonogashira* coupling of the acetylene **1** and the iodide **2** in the presence of 5% $[Pd_2(dba)_3]$, 7% CuI and 7% $P(fur)_3$ to yield 77% of the dimer **4** [4] (*Scheme 1*). *C*-Desilylation of **4** led in 63% yield[1]) to the dimeric acetylene **5** [4]. In the second cycle, the iodide **2** was coupled to the dimer **5** to yield 63% of the trimer **6**. Yields dropped significantly in the following coupling of **2** with **7** to the tetramer **8**. We, therefore, reinvestigated the reaction conditions for this step (*Table 1*).

As shown in *Table 1*, complete conversion of the alkyne **7** required large amounts of Pd catalyst. Yields remained low, and the coupling product **8** was not readily separated from **7**[2]). Replacing Et_3N with 2,2,6,6-tetramethylpiperidine (TMP), or substituting toluene with DMSO or DMF led to a complex mixture containing small amounts of **8**. Lower yields resulted from replacing $P(fur)_3$ by $P(i\text{-}Pr)_3$ or $Ph_2P(CH_2)_nPPh_2$ ($n = 2$, 3, or 5). *C*-Desilylation of **8** yielded 54% of the alkyne **9** that was coupled with 3 equiv. of the iodide **2** in the presence of 0.5 equiv. of $[Pd_2(dba)]_3$ and 1 equiv. each of CuI and $P(fur)_3$ to yield 15% of the pentamer **10** that was *C*-desilylated to the alkyne **11** (52%; *Table 2*). Analogous conditions were used for the coupling of the iodouracil **3** with the dimer **5**, trimer **7**, tetramer **9**, and pentamer **11** to yield the products **12**–**14** in yields of

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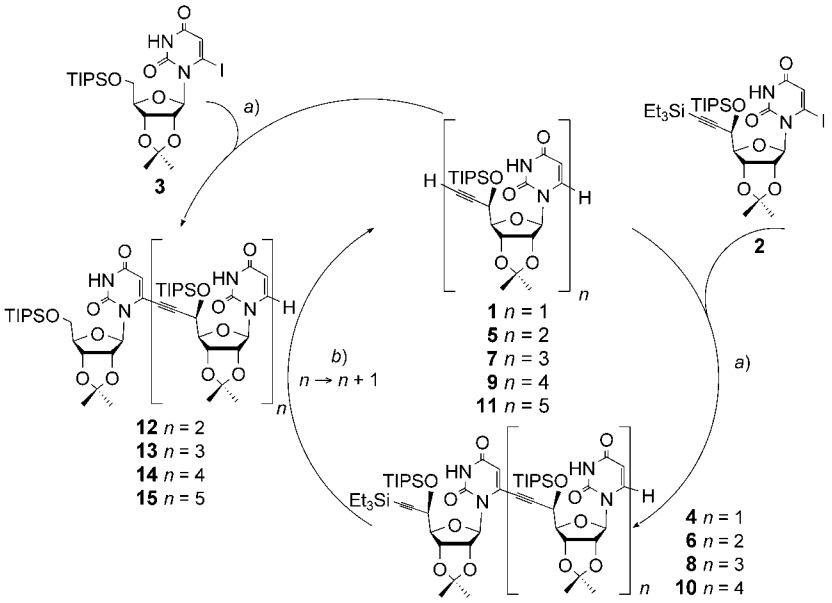
[1]) When the HO–C(5′) groups were protected as Et_3Si-ethers instead of $(i\text{-}Pr)_3Si$ (TIPS)-ethers it was not possible to *C*-desilylate under these conditions without partial desilylation of the Et_3Si ethers.

[2]) Coupling of **7** to the propargylic alcohol corresponding to **2** led in lower yields (*ca.* 10%) to a more readily separated mixture of **7** and coupling product [4].

Scheme 1



a) $[Pd_2(dba)_3]$ (dba = dibenzylideneacetone = 1,5-diphenylpenta-1,4-dien-3-one), CuI, $P(fur)_3$, toluene/Et_3N 1:1. *b*) $AgNO_3$, MeOH/AcOEt, then KCN.

Table 1. *Cross-Coupling of the Iodide* **2** *with the Trimer* **7**: *Reaction Conditions and Yields of* **8**

Entry	Equiv. of **7**	Equiv. of $[Pd_2(dba)_3]$/CuI/PX_3	Base, solvent	Time [h]	Yield of **8** [%]
1	4	0.4/0.4/0	Et_3N, toluene	100	40[a])
2	2	0.4/0.8/0.8 (X = fur)	Et_3N, toluene	48	40[a])
3	3	0.6/1.2/1.2 (X = fur)	Et_3N, toluene	120	18
4	2	0.5/1.0/1.0 (X = fur)	TMP, toluene	72	mixture[b])
5	2	0.5/1.0/1.0 (X = fur)	Et_3N, DMF	72	0
6	2	0.5/1.0/1.0 (X = fur)	Et_3N, DMSO	72	mixture[b])
7	3	0.4/0.8/0.8 (X = i-Pr)	Et_3N, toluene	72	traces[b])
8	3	0.4/0.8/1.0 [c])	Et_3N, toluene	72	traces[b])

[a]) Less than 50% conversion. [b]) Compound **8** was detected by MALDI-TOF-MS of the crude after a small-scale workup. [c]) $PX_3 = Ph_2P(CH_2)_nPPh_2$ ($n = 2$, 3, or 5).

57, 25, and 11%, respectively. The desired hexamer **15** was only formed in trace amounts, denoting the practical limits of the linear approach.

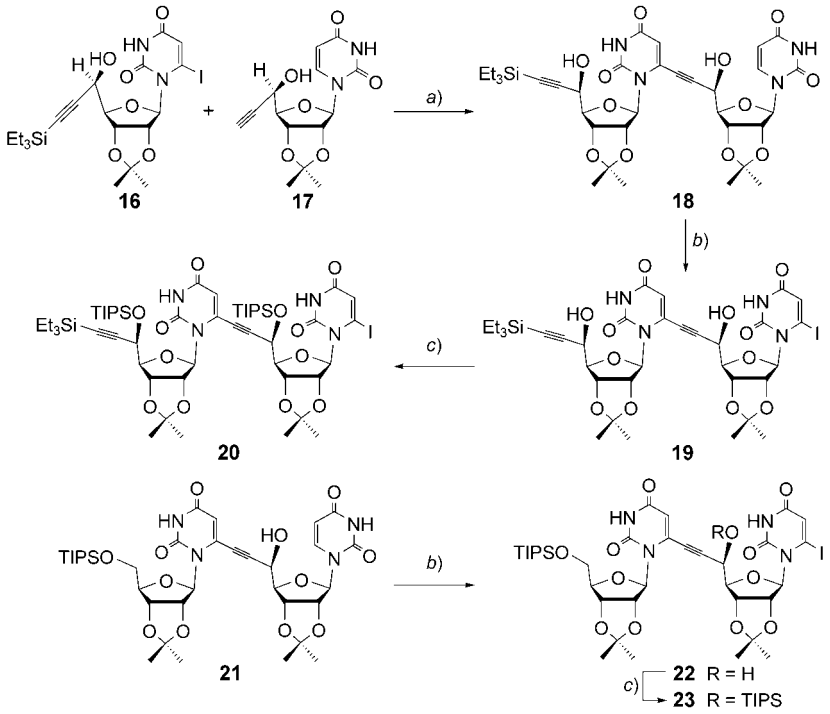
To reduce the number of coupling steps and to alleviate the separation problem, we also investigated a convergent approach, *i.e.*, coupling of the iodinated dimers **20** and **23** (*Scheme 2*) with the dimer **5**, trimer **7**, and tetramer **9** (*Scheme 3*). Coupling of the alkyne **17** [4] with the iodide **16** [4] yielded 91% of the dimer **18**, which was iodinated at C(6/I) by treatment with a large excess of LDA and then NIS (*Scheme 2*). This

Table 2. *Conditions and Yields of the Cross-Coupling of the Iodides* **2** *and* **3** *with the Acetylenes* **1**, **5**, **7**, **9**, *and* **11**, *and of the* C*-Desilylation of* **4**, **6**, **8**, *and* **10**

	n	$[Pd_2(dba)_3]$ [mol-%]	Equiv. of alkyne	Reaction time [h]	Yield of coupling	Equiv. of KCN/$AgNO_3$	Yield of desilylation
Dimer	1	5	**2**: 1.1	80	77% of **4**	10/30	63% of **5**
Trimer	2	20	**2**: 1.4	80	63% of **6**	10/30	87% of **7**
		10	**3**: 1.2	40	57% of **12**		
Tetramer	3	60	**2**: 3.1	100	18% of **8**	20/50	54% of **9**
		38	**3**: 3.3	100	25% of **13**		
Pentamer	4	50	**2**: 3.0	100	15% of **10**	60/150	52% of **11**
		40	**3**: 2.5	125	11% of **14**		
Hexamer	5	100	**3**: 2.0	100	traces of **15**[a])		

[a]) A signal of **15** was found in the MALDI-TOF mass spectrum of the crude after a small-scale workup.

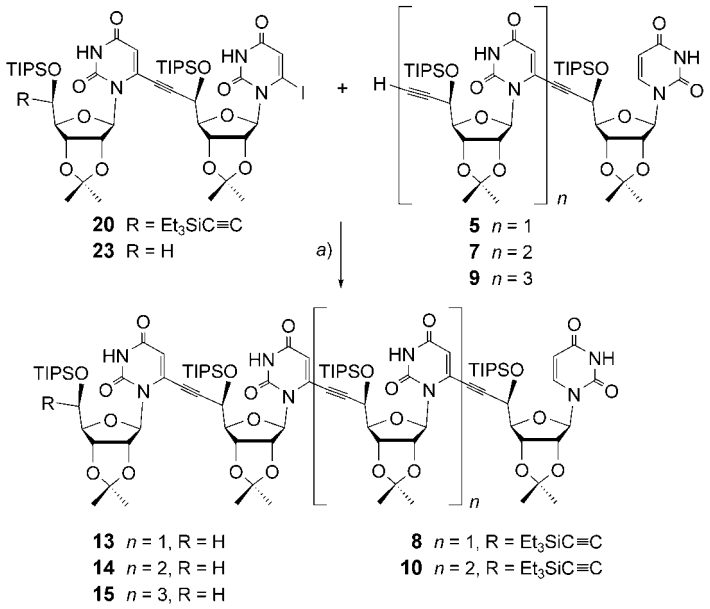
Scheme 2



a) $[Pd_2(dba)_3]$, CuI, $P(fur)_3$, toluene/Et_3N 1:1; 91%. *b*) Lithium diisopropylamide (LDA), THF, then *N*-iodosuccinimide (NIS), then AcOH; 40% of **19**; 40% of **22**. *c*) Triisopropylsilyl trifluoromethanesulfonate (TIPSOTf), 2,6-di(*tert*-butyl)pyridine, CH_2Cl_2; 62% of **20**; 50% of **23**.

provided the iodide **19** (40%) besides 20% of starting material. As expected (*cf.* [4]), lithiation appears to be promoted by the propargylic OH group; scouting experiments showed that the TIPS–O(5′) protected derivative of **18** decomposed under the same reaction conditions. Lithiation of **18** with lithium 2,2,6,6-tetramethylpiperidide

Scheme 3



a) $[Pd_2(dba)_3]$, CuI, $P(fur)_3$, toluene/Et_3N 1:1.

(LiTMP), followed by iodination, led to similar results as treatment with LDA and NIS, while lithiation with LiTMP in the presence of HMPT, followed by treatment with NIS, gave no conversion. Attempted silylation of the iodide **19** with TIPSOTf and pyridine in CH_2Cl_2 led to decomposition, while silylation with TIPSOTf and 2,6-di(*tert*-butyl)pyridine [11] gave 62% of the silyl ether **20**. The iodide **23** was required to introduce an terminal unit devoid of the *C(5′)*-ethynyl substituent; it was obtained similarly to **19** in a yield of 20% from the known dimer **21** [4]. The low yields in the iodination of the dimer **18** did not augur well for the iodination of higher oligomers, and, since a binomial synthesis requires an iodination step after each reaction cycle, we restricted our investigation of the convergent synthesis to coupling of the iodides **20** and **23** with the acetylenes **5**, **7**, and **9**.

The results of coupling the iodinated dimers **20** and **23** with the acetylenes **5**, **7**, and **9** (*Scheme 3*) are summarised in *Table 3*. Although this strategy provided hexamer **15**, coupling required excess of the iodides and high concentrations of Pd catalyst to ensure a complete conversion of the alkyne. Yields decreased considerably from coupling the iodides **20** and **23** with the alkyne **5** to the tetramers **8** and **13**, to coupling with the alkyne **7** to the pentamers **10** and **14**, and further to coupling of **23** with **9** to **15** that was isolated in a yield of barely 5%. The synthesis of the pentamers **10** and **14** by the convergent synthesis was difficult to reproduce, and the products were only separated with difficulty from the starting alkyne. To facilitate the isolation of the products, we coupled the HO–C(5′) unprotected iodinated dimers **19** and **22** with **5**, **7**, and **9** so as to increase the polarity difference between coupling product and starting alkyne.

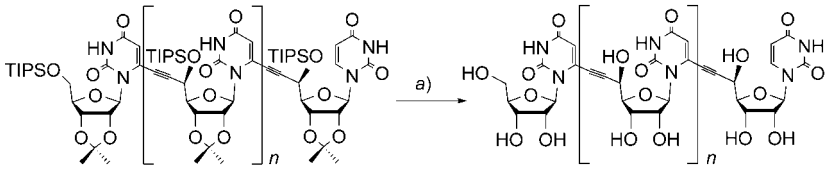
Table 3. *Conditions and Yields of the Cross-Coupling of the Dimeric Iodides* **20** *and* **23** *with the Acetylenes* **5**, **7**, *and* **9**

	n	Alkyne	[$Pd_2(dba)_3$] [mol-%]	Equiv. of iodide	Reaction time [h]	Yield
Tetramer	1	**5**	20	**20**: 1.5	120	36% of **8**
		5	20	**23**: 1.5	100	51% of **13**
Pentamer	2	**7**	40	**20**: 2.0	100	20% of **10**
		7	38	**23**: 2.0	100	15% of **14**
Hexamer	3	**9**	90	**23**: 4.0	170	5% of **15**

However, this led to a more-complex reaction mixture and lowered the yield of the coupling products.

Treatment of the trimer **12**, tetramer **13**, and pentamer **14** with 0.16N HCl and 0.3N HF in H_2O/MeCN 2:1 [12] led in one step and in yields of 58–70% to the uridine-derived oligomers **24**–**26**, respectively (*Scheme 4*).

Scheme 4



12 *n* = 1
13 *n* = 2
14 *n* = 3

24 *n* = 1
25 *n* = 2
26 *n* = 3

a) H_2O/MeCN/37% HCl/40% HF 100:50:2:2; 70% of **24**, 67% of **25**, 58% of **26**.

The ^{1}H-NMR assignment of the dimers **18**, **19**, **20**, **22**, and **23** is corroborated by selective homodecoupling experiments (see *Table 5* in the *Exper. Part*). The downfield shift of 0.16 ppm for H–C(2′/I) of **18** relative to the monomer **17** indicates a 1:1 *syn*/*anti* equilibrium [13] for unit I (the alkynylated uridine unit; see [4] for the nomenclature of the chain numbering) in **18**. Similarly, the downfield shift of H–C(2′/I) (0.19 and 0.27 ppm) of **4** and **5** relative to the monomer **1** indicates a 1:1 *syn*/*anti* equilibrium for unit I in **4** and **5**. The downfield shift for H–C(2′/I) ($\Delta\delta$ = 0.51–0.59 ppm) of the iodinated dimers **19**, **20**, **22**, and **23** relative to **1** evidences a *syn*-conformation of the nucleobase in unit I. The chemical shifts for H–C(2′/II) in all dimers correspond to the chemical shifts for H–C(2′/I) of the iodinated dimers ($\Delta\delta \leq$ 0.10 ppm) and indicates a *syn*-conformation also of the nucleobase in unit II of the dimers. A ratio $J(1',2')/J(3',4')$ of 0.24–0.74 in both subunits indicates a preference for the $^3T_2$ conformation of the sugar pucker [13].

The large $J(4',5')$ of 5.6–8.6 Hz for unit II of **4**, **5**, and **18**–**20**, and for unit I in the iodinated dimers **19**, **20**, **22**, and **23** indicate a steric interaction between the nucleobase and the side chain at C(4′); the conformer possessing antiperiplanar H–C(4′) and H–C(5′) bonds is favoured. $J(4',5')$ value of unit I in the non-iodinated dimers **4**, **5**, and **18** is significantly smaller (4.6–5.5 Hz). In the ^{13}C-NMR spectra (see *Table 6* in the *Exper. Part*), introduction of I–C(6) leads to an upfield shift of C(6/I) of **19**, **20**, **22**, and

23, resonating at 114–117 ppm ($\Delta\delta$ = 28 ppm) and to a downfield shift of C(5/I), resonating at 117 ppm ($\Delta\delta$ = 15 ppm) and C(1′/I) at 102–104 ppm ($\Delta\delta$ = 7 ppm), as it was already observed for the *C(6)*-iodinated monomers [4]. The ^{13}C-NMR spectra of all iodinated dimers showed the expected shifts for C(2′) (84–86 ppm), C(3′) (81–84 ppm), C(4′) (90–92 ppm), and C(5′) (63–64 ppm). The *s*s for C(6′) and C(7′) of the C≡C–$SiEt_3$ groups of **4** and **18**–**20** appear at 106.3–107.3 and 87.8–88.2 ppm, and the *s*s for C(6′) and C(7′) of the bridging C≡C units at 100.4–102.2 and 75.8–76.9 ppm, respectively.

A downfield shift for H–C(2′/I) of 0.24–0.34 ppm for all protected trimers, tetramers, and pentamers, and a downfield shift of 0.47–0.52 ppm for H–C(2′/II–V) relative to the monomer **1** evidence again a 1:1 *syn*/*anti* equilibrium for unit I and a preferred *syn*-conformation for the units II–IV (see *Tables 7*, *9*, and *11* in the *Exper. Part*). The ratio of $J(1',2')$ = 0–1.9 to $J(3',4')$ = 2.8–5.6 Hz indicates a preference for the $^3T_2$ sugar pucker. The large $J(4',5')$ = 5.0–8.0 Hz suggests a preponderant antiperiplanar arrangement of H–C(4′) and H–C(5′), as observed for the iodinated dimers. All ^{13}C-NMR signals of the tri- and tetramers resonate at the expected field (see *Tables 8* and *10* in the *Exper. Part*); C(1′) at 94.1–95 ppm and C(2′)–C(5′) as indicated above for the dimers. The C≡CH group of **5**, **7**, and **9** resonates at 73.7–73.1 for C(7′)[3]) and at 83.8 ppm for C(6′). The signals for the C≡C$SiEt_3$ and the bridging ethynylene groups appear in the range given for the dimers.

Similarly as for the fully protected analogues, H–C(2′) of the deprotected **24**–**26** resonate downfield (by 0.2–0.3 ppm for unit I and by 0.54–0.71 ppm for units II–V) as compared to the deprotected monomer of **1** [4], indicating a 1:1 *syn*/*anti* equilibrium for unit I and a preferred *syn*-conformation of units II–V (see *Table 12* in the *Exper. Part*). The ratio of $J(1',2')$ = 3.6–6.0 to $J(3',4')$ = 3.2–5.8 Hz indicates a 1:1 mixture of the $^3T_2$ and $^2T_3$ conformers for all units. In the ^{13}C-NMR spectra of **24** and **25** (see *Tables 8* and *10* in the *Exper. Part*), one notes the expected upfield shift for C(2′/I–IV) and C(3′/I–IV) (7.6–11.0 ppm) and smaller shifts ($\Delta\delta < 2$ ppm) for the other C-atoms. The *syn*-conformation (χ = 45–75°) is not in agreement with the χ angles of 115–145° or −45 to −75° that our model studies suggested to be required for duplex formation. According to these studies, **24**–**26** are not preorganized for duplex formation and are not expected to pair strongly.

The RNA strands rA_5, rA_7, rU_5, and rU_7 (*Table 4*) that we required for first UV melting experiments of a potential duplex with the pentamer **26** (**26**·rA_5 and **26**·rA_7) as compared to RNA duplexes ($rU_5 \cdot rA_5$ and $rU_7 \cdot rA_7$) were prepared by solid-phase synthesis according to [15].

Neither the 15:15 μmol mixtures of the pentamer **26** and the RNA strand A_5 or A_7, nor the mixtures A_5 and U_5, nor A_7 and U_5 showed any sigmoid UV melting curve in a 10-mmol NaH_2PO_4/Na_2HPO_4 buffer at pH 7 and at a 0.2M concentration of NaCl (*Fig. 2*). A first indication for a sigmoid curve was only visible in the temperature-dependent UV curve of the RNA duplex $rA_7 \cdot rU_7$, indicating that the pentamer **26** does not bind to RNA more strongly than the RNA strand rU_5.

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[3]) Surprisingly, both C-atoms of terminal alkynes display in the DEPT spectrum a very weak signal; see [14].

Table 4. *Synthesis and Characterisation of rA_5, rA_7, rU_5, and rU_7*

Product	Sequence	Yield [%]		Molecular formula	$[M-H]^-$ c)	
		a)	b)		calc.	obs.
rA_5	5′-r(AAAAA)-3′	> 99	6	$C_{50}H_{61}N_{25}O_{28}P_4$	1584.1	1583.5
rA_7	5′-r(AAAAAAA)-3′	99	5	$C_{70}H_{85}N_{35}O_{40}P_6$	2242.6	2242.2
rU_5	5′-r(UUUUU)-3′	96	8	$C_{45}H_{56}N_{10}O_{38}P_4$	1469.0	1467.3
rU_7	5′-r(UUUUUUU)-3′	94	4	$C_{63}H_{78}N_{14}O_{54}P_6$	2081.4	2080.4

a) Calculated from the yield of the coupling steps, as determined by the detritylation assay. b) Yield after purification. c) Determined by MALDI-TOF mass spectrometry according to [16].

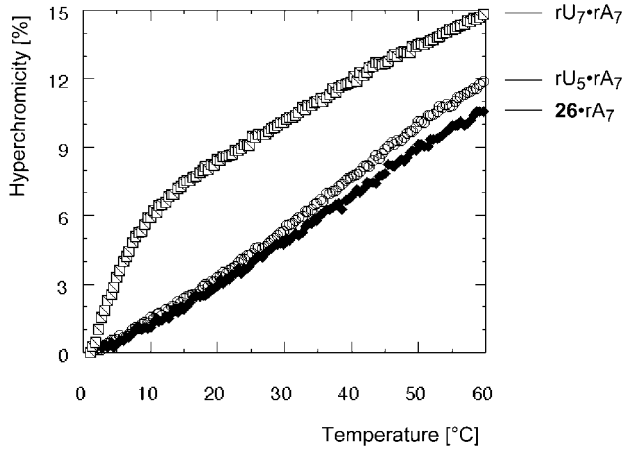

Fig. 2. *Temperature-dependent UV spectra* ('melting curves') *of* **26**$\cdot(rA_7)$, $(rU_5)\cdot(rA_7)$, *and* $(rU_7)\cdot(rA_7)$

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

Experimental Part

General. Solvents were distilled: 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: Fast-atom-bombardment (FAB; NOBA: 3-nitrobenzyl alcohol), electron spray ionisation (ESI), or HR-MALDI (DHB: 2,5-dihydroxybenzoic acid).

*1-[6,7-Dideoxy-2,3-*O*-isopropylidene-7-*C*-(triethylsilyl)-5-*O*-(triisopropylsilyl)-β-*D*-*allo*-hept-6-ynofuranosyl]uracil-6-yl-(6→7′-*C*)-1-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triisopropylsilyl)-β-*D*-*allo*-hept-6-ynofuranosyl]uracil-6-yl-(6→7′-*C*)-1-[6,7-dideoxy-2,3-*O*-isopropylidene-5-*O*-(triisopropylsilyl)-β-*D*-*allo*-hept-6-ynofuranosyl]uracil* (**6**). A soln. of **5** [4] (1.1 g, 1.2 mmol), **2** [4] (1.2 g, 1.7 mmol), $[Pd_2(dba)_3]$ (228 mg, 0.24 mmol), CuI (68 mg, 0.36 mmol), and $P(fur)_3$ (83 mg, 0.36 mmol) in degassed Et_3N/toluene 1:1 (40 ml) was stirred for 80 h at 23°. After evaporation, FC (AcOEt/hexane 1:3→1:1) gave **6** (1.13 g, 63%). Brown foam. R_f (AcOEt/hexane 1:1) 0.23. $[\alpha]_D^{25} = +7.6$ ($c = 0.8$, $CHCl_3$). IR ($CHCl_3$): 3373*m* (br.), 3192*m* (br.), 2949*m*, 2869*w*, 2233*w*, 2178*w*, 1699*s*, 1597*w*, 1455*m*, 1382*m*, 1216*m*, 1091*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 5*; additionally, 9.85,

9.47, 9.35 (3 br. *s*, 3 NH); 1.57, 1.55, 1.51, 1.36, 1.33, 1.32 (6*s*, 3 Me_2C); 1.23–1.15 (*m*, 3 $(Me_2CH)_3Si$); 1.13–1.08 (*m*, 3 $(Me_2CH)_3Si$); 0.93 (*t*, *J* = 7.8, $(MeCH_2)_3Si$); 0.55 (*q*, *J* = 7.8, $(MeCH_2)_3Si$). ^{13}C-NMR (125 MHz, $CDCl_3$): see *Table 6*, additionally, 114.8, 113.9, 113.3 (3*s*, 3 Me_2C); 27.22, 27.20, 27.1, 25.4, 25.1, 25.0 (6*q*, 3 Me_2C); 18.10, 18.08, 18.0 (6 C), 17.97, 17.96 (5*q*, 3 $(Me_2CH)_3Si$); 12.5, 12.4, 12.3 (3*d*, 3 $(Me_2CH)_3Si$); 7.3 (*q*, $(MeCH_2)_3Si$); 4.2 (*t*, $(MeCH_2)_3Si$). HR-MALDI-MS (DHB): 1525.748 ($[M + Na]^+$, $C_{75}H_{118}Si_4N_6NaO_{18}^+$; calc. 1525.748).

Table 5. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Trimers* **6**, **7**, *and* **12** *in $CDCl_3$* (assignment based on selective homodecoupling experiments)

	6	**7**	**12**		**6**	**7**	**12**
H–C(5/I)	5.72	5.72	5.73	*J*(1′,2′/I)	1.2	1.0	0
H–C(5/II–III)	6.03, 5.99	6.03, 6.00	6.01, 5.98	*J*(1′,2′/II–III)	1.0,	1.3,	0,
H–C(6/I)	7.31	7.30	7.31		1.9	0	1.3
H–C(1′/I)	5.73	5.71	5.72	*J*(2′,3′/I–III)	[a])	[a])	[a])
H–C(1′/II–III)	6.18, 6.17	6.20, 6.18	6.21, 6.18		6.5,	6.0,	5.8,
H–C(2′/I)	5.00–4.98	5.07–4.96	5.02–4.98		6.4	6.2	6.0
H–C(2′/II–III)	5.25, 5.21	5.22, 5.21	5.22, 5.20	*J*(3′,4′/I)	3.4	2.8	[a])
H–C(3′/I–II)	5.02–4.98	5.07–4.96	5.02–4.98	*J*(3′,4′/II)	4.5	4.5	4.6
H–C(3′/III)	5.05	5.07–4.96	4.85	*J*(3′,4′/III)	3.8	3.8	4.6
H–C(4′/I–II)	4.21, 4.08	4.21, 4.08	4.22, 4.08	*J*(4′,5′/I)	5.2	5.6	8.0
H–C(4′/III)	4.01	4.05	4.14	*J*(4′,5′/II)	6.5	6.5	8.0
H–C(5′/I)	5.06	5.06	5.06	*J*(4′,5′/III)	7.5	7.6	6.2
H–C(5′/II)	4.99	4.99	5.00				
H–C(5′/III)	4.64	4.64	3.86 (2 H)				

[a]) Not assigned.

Table 6. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Trimers* **6**, **7**, *and* **12** *in $CDCl_3$, and* of **24** *in D_2O Solution*

	6	**7**	**12**	**24**
C(2/I–III)	163.3, 162.6, 162.5	163.2, 162.7, 162.5	163.4, 163.0, 162.7	168.7, 167.5, 167.4
C(4/I–III)	149.9, 149.6, 149.4	149.8, 149.6, 149.4	149.91, 149.88, 149.4	154.3, 153.4, 153.0
C(5/I–III)	108.7, 108.3, 102.7	108.6, 108.4, 102.7	108.5, 108.2, 102.6	111.1, 111.0, 105.2
C(6/I–III)	142.2, 138.0, 137.3	142.2, 138.0, 137.3	142.3, 138.0, 137.4	144.6, 140.74, 140.70
C(1′/I–III)	94.3, 94.23, 94.16	94.4, 94.3, 94.2	94.4, 94.1, 93.9	96.8, 96.7, 92.0
C(2′/I–III)	84.0, 83.9, 83.8	84.2, 83.8, 83.7	84.5, 83.9, 83.7	75.8, 74.1, 73.5
C(3′/I–III)	82.8, 82.1, 80.6	82.8, 82.2, 80.7	82.3, 82.0, 80.7	73.1, 72.7, 71.9
C(4′/I–III)	91.2, 90.1, 88.7	91.4, 90.1, 88.7	90.0, 89.9, 88.7	88.0, 87.5, 86.6
C(5′/I–III)	64.3, 63.9, 63.8	64.3, 63.8, 63.4	64.6, 64.4, 63.8[a])	65.1, 64.8, 64.0[a])
C(6′/I–II)	101.5, 100.8	101.5, 100.9	101.5, 100.9	102.9, 102.6
C(6′/III)	106.5	83.8	–	–
C(7′/I–III)	87.7, 76.5, 75.9	76.5, 75.9, 73.7	76.5, 76.0, –	79.0, 78.6, –

[a]) *t* of C(5′/III).

1-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6→7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6→7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**7**). A soln. of **6** (1.8 g, 1.2 mmol) in MeOH/AcOEt 1:1 (300 ml) was treated dropwise with a soln. of $AgNO_3$ (2.4 g, 49.5 mmol) in H_2O/MeOH 1:1 (30 ml), stirred at 23° under exclusion of light for 4 h, treated with a soln. of KCN (2.8 g) in H_2O (10 ml), and stirred for 1 h. After evaporation, a soln. of the residue in AcOEt was washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:3→2:1) gave **7** (1.45 g, 87%). Yellow foam.

R_f (AcOEt/hexane 1:1) 0.22. $[\alpha]_D^{25} = +2.1$ ($c = 0.7$, CH_2Cl_2). IR ($CHCl_3$): 3372*w* (br.), 3301*w*, 2947*m*, 2868*m*, 2233*w*, 1700*s*, 1597*w*, 1454*m*, 1381*m*, 1091*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 5*; additionally, 9.90, 9.48 (2 H) (2 br. *s*, 3 NH); 2.40 (*d*, $J = 2.0$, H–C(7′/III)); 1.57, 1.55, 1.51, 1.36, 1.33, 1.32 (6*s*, 3 Me_2C); 1.23–1.08 (*m*, 3 (Me_2CH)$_3$Si). ^{13}C-NMR (125 MHz, $CDCl_3$): see *Table 6*; additionally, 114.8, 113.9, 113.3 (3*s*, 3 Me_2C); 27.23, 27.21, 27.1, 25.4, 25.1, 25.0 (6*q*, 3 Me_2C); 18.10 (6 C), 18.08, 18.00, 17.97, 17.96 (5*q*, 3 (Me_2CH)$_3$Si); 12.5, 12.4, 12.3 (3*d*, 3 (Me_2CH)$_3$Si). HR-MALDI-MS (DHB): 1141.660 ($[M + Na]^+$, $C_{69}H_{104}N_6NaO_{18}Si_3^+$; calc. 1411.661).

1-[6,7-Dideoxy-2,3-O-*isopropylidene-7*-C-*(triethylsilyl)-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_2$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**8**). a) *From* **7** *and* **2**. A soln. of **7** (100 mg, 72 μmol), **2** (150 mg, 0.22 mmol), [Pd_2(dba)$_3$] (41.3 mg, 43 μmol), CuI (16 mg, 86 μmol), and P(fur)$_3$ (20 mg, 86 μmol) in degassed Et_3N/toluene 1:1 (7 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:2 → 1:1) gave **8** (25 mg, 18%).

b) *From* **5** *and* **20**. A soln. of **5** (30 mg, 32 μmol), **20** (57 mg, 49 μmol), [Pd_2(dba)$_3$] (6.3 mg, 6.4 μmol), CuI (1.8 mg, 9.4 μmol), and P(fur)$_3$ (2.2 mg, 9.4 μmol) in degassed Et_3N/toluene 1:1 (6 ml) was stirred for 120 h at 23°. After evaporation, FC (AcOEt/hexane 1:2 → 1:1) and prep. TLC (AcOEt/hexane 1:1) gave **8** (23 mg, 36%). Yellow foam. R_f (AcOEt/hexane 1:1) 0.23. $[\alpha]_D^{25} = +2.6$ ($c = 0.3$, $CHCl_3$). IR ($CHCl_3$): 3375*m* (br.), 3192*w* (br.), 2949*m*, 2868*m*, 2235*w*, 1699*s*, 1596*w*, 1456*m*, 1384*m*, 1215*m*, 1092*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 7*; additionally, 9.90, 9.80, 9.30, 9.00 (4 br. *s*, 4 NH); 1.56, 1.55, 1.54, 1.51, 1.36, 1.35, 1.33, 1.32 (8*s*, 4 Me_2C); 1.23–1.15 (*m*, 4 (Me_2C*H*)$_3$Si); 1.13–1.08 (*m*, 4 (Me_2CH)$_3$Si); 0.94 (*t*, $J = 7.5$, ($MeCH_2$)$_3$Si); 0.55 (*q*, $J = 7.5$, (MeCH_2)$_3$Si). ^{13}C-NMR (125 MHz, $CDCl_3$): see *Table 8*; additionally, 114.7, 114.0, 113.9, 113.3 (4*s*, 4 Me_2C); 27.2 (3 C), 27.1, 25.35, 25.23, 25.07, 25.04 (6*q*, 4 Me_2C); 18.10, 18.08, 18.02, 17.97 (4*q*, 4 (Me_2CH)$_3$Si); 12.5, 12.34 (6 C), 12.30 (3*d*, 4 (Me_2CH)$_3$Si); 7.3 (*q*, ($MeCH_2$)$_3$Si); 4.2 (*t*, (MeCH_2)$_3$Si). HR-MALDI-MS (DHB): 1987.967 ($[M + Na]^+$, $C_{98}H_{152}N_8NaO_{24}Si_5^+$; calc. 1987.966).

Table 7. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Tetramers* **8**, **9**, *and* **13** *in $CDCl_3$*

	8	**9**	**13**
H–C(5/I)	5.72	5.75	5.75
H–C(5/II–IV)	6.12, 6.02, 6.00	6.13, 6.06, 6.01	6.11, 6.05, 5.99
H–C(6/I)	7.28	7.28	7.28
H–C(1′/I)	5.64	5.65	5.66
H–C(1′/II–IV)	6.19 (2 H), 6.17	6.22, 6.19, 6.13	6.25, 6.19, 6.17
H–C(2′/I)	5.07–4.96	5.06–4.96	5.01–4.98
H–C(2′/II–IV)	5.23–5.19	5.23–5.19	5.23–5.19
H–C(3′/I–IV)	5.07–4.96	5.06–4.96	5.01–4.98, 4.78[a])
H–C(4′/I–III)	4.19, 4.08, 4.07	4.20, 4.07, 4.05	4.20, 4.14, 4.08
H–C(4′/IV)	4.00	4.03	4.08
H–C(5′/I–III)	5.06, 5.03, 4.99	5.06–4.96	5.06, 5.03, 5.00
H–C(5′/IV)	4.64	4.62	3.85 (2 H)
J(1′,2′/I)	1.9	1.8	1.4
J(1′,2′/II–IV)	0.0, 1.1, 0.0	1.0, 1.5, 1.0	0.0, 1.2, 1.0
J(2′,3′/I–IV)	6.4, 6.4, [b]), [b])	[b])	[b])
J(3′,4′/I–IV)	3.8, 4.0, 4.6, 3.6	4.0, 5.6, 1.7, 3.9	[b])
J(4′,5′/I–III)	5.3, 6.6, 7.2	5.3, 6.9, 4.8	[b])
J(4′,5′/IV)	8.0	8.5	7.3

[a]) H–C(3/IV). [b]) Not assigned.

1-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_2$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**9**). A soln. of **8** (39 mg, 20 μmol) in MeOH/AcOEt 1:1 (20 ml) was treated dropwise with a soln. of $AgNO_3$

Table 8. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Tetramers* **8**, **9**, *and* **13** *in $CDCl_3$, and of* **25** *in D_2O Solution*

	8	**9**	**13**	**25**
C(2/I–IV)	163.1, 162.7, 162.4, 162.3	163.4, 163.0, 162.7, 162.6	163.6, 163.5, 163.0, 162.8	168.6, 167.42, 167.39, 167.2
C(4/I–IV)	149.7, 149.6, 149.42, 149.41	149.8, 149.7, 149.6, 149.5	150.1, 149.8, 149.51, 149.48	154.2, 153.3, 153.1, 153.0
C(5/I–IV)	108.7, 108.6, 108.4, 102.6	108.7, 108.6, 108.4, 102.7	108.6, 108.5, 108.3, 102.7	111.1, 110.93, 110.89, 105.2
C(6/I–IV)	142.5, 138.0, 137.7, 137.3	142.5, 137.9, 137.7, 137.3	142.5, 137.9, 137.7, 137.4	144.6, 140.8, 140.7, 140.6
C(1′/I–IV)	95.0, 94.3, 94.2, 93.9	94.8, 94.1, 94.0, 93.6	94.7, 94.0, 93.7, 93.2	96.5 (2 C), 92.0 (2 C)
C(2′/I–IV)	84.0, 83.8 (2 C), 83.7	84.5, 83.9, 83.8, 83.6	83.9, 83.8 (2 C), 83.6	75.7, 74.1, 73.54, 73.48
C(3′/I–IV)	82.7, 82.2, 82.1, 80.9	82.8, 82.7, 81.9, 80.8	82.2, 81.9, 81.6, 80.8	73.2, 73.0, 72.6, 71.8
C(4′/I–IV)	91.1, 90.1, 89.7, 87.7	91.3, 89.9, 89.8, 88.9	89.9, 89.6, 88.9, 84.6	88.0, 87.64, 86.61, 86.5
C(5′/I–IV)	64.4 (2 C), 63.90, 63.86	64.4 (2 C), 63.8, 63.4	64.6, 64.44, 64.38, 63.8[a])	65.09, 65.06, 64.8, 63.9[a])
C(6′/I–III)	101.6, 101.5, 100.9	101.6, 101.4, 100.9	101.2, 101.02 (2 C)	103.2, 103.0, 102.6
C(6′/IV)	106.4	83.8	–	–
C(7′/I–IV)	88.8, 76.4, 75.8 (2 C)	76.4, 75.8 (2 C), 73.1	76.0, 75.9, 76.5, –	79.0, 78.6 (2 C), –

[a]) *t* of C(5′/IV).

(67 mg, 0.4 mmol) in H_2O/MeOH 1:1 (2 ml), stirred at 23° under exclusion of light for 5 h, treated with a soln. of KCN (67 mg, 1 mmol) in H_2O (1 ml), and stirred for 3 h. After evaporation, a soln. of the residue in AcOEt was washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:1 → 2:1) gave **9** (20 mg, 54%). Yellow foam. R_f (AcOEt/hexane 1:1) 0.22. $[\alpha]_D^{25} = 2.7$ ($c = 0.7$, CH_2Cl_2). IR ($CHCl_3$): 3372*w* (br.), 3301*w*, 3193*w*, 3068*w*, 2947*m*, 2868*m*, 2234*w*, 1699*s*, 1597*w*, 1455*m*, 1382*m*, 1090*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 7*; additionally, 10.05 (br. *s*, 2 NH); 9.42 (br. *s*, 2 NH); 2.41 (*d*, $J = 2.0$, H–C(7′/IV)); 1.57, 1.56, 1.54, 1.52, 1.36, 1.34, 1.33, 1.32 (8*s*, 4 Me_2C); 1.21–1.08 (*m*, 4 $(Me_2CH)_3Si$). ^{13}C-NMR (100 MHz, $CDCl_3$): see *Table 8*; additionally, 114.66, 114.02, 113.9, 113.4 (4*s*, 4 Me_2C); 27.25, 27.21, 27.18, 27.11, 25.4, 25.3, 25.10, 25.08 (8*q*, 4 Me_2C); 18.03 (12 C), 18.00, 17.96 (3*q*, 4 $(Me_2CH)_3Si$); 12.4, 12.32 (6 C), 12.27 (3*d*, 4 $(Me_2CH)_3Si$). HR-MALDI-MS (DHB): 1873.879 ($[M + Na]^+$, $C_{92}H_{138}N_8NaO_{24}Si_4^+$; calc. 1873.880).

1-[6,7-Dideoxy-2,3-O-*isopropylidene-7*-C-*(triethylsilyl)-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_3$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**10**). a) *From* **9** *and* **2**. A soln. of **9** (20 mg, 11 μmol), **2** (23 mg, 32 μmol), $[Pd_2(dba)_3]$ (5 mg, 11 μmol), CuI (2.1 mg, 11 μmol), and $P(fur)_3$ (2.5 mg, 11 μmol) in degassed Et_3N/toluene 1:1 (3 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:2 → 1:1) and prep. TLC (AcOEt/hexane 1:1) gave **10** (4 mg, 15%).

b) *From* **7** *and* **20**. A soln. of **7** (20 mg, 14 μmol), **20** (34 mg, 29 μmol), $[Pd_2(dba)_3]$ (5.5 mg, 5.8 μmol), CuI (1.6 mg, 8.6 μmol), and $P(fur)_3$ (2.0 mg, 8.6 μmol) in degassed Et_3N/toluene 1:1 (6 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:2 → 1:1) and prep. TLC (AcOEt/hexane 1:1) gave **10** (7 mg, 20%). Yellow foam. R_f (AcOEt/hexane 1:1) 0.23. $[\alpha]_D^{25} = 5.1$ ($c = 1.3$, $CHCl_3$). IR (CH_2Cl_2): 3372*m* (br.), 3193*m* (br.), 2946*m*, 2235*w*, 1699*s*, 1595*w*, 1457*m*, 1384*m*, 1214*m*, 1091*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 9*; additionally, 10.12 (br. *s*, 3 NH); 9.42 (br. *s*, 2 NH); 1.56, 1.55, 1.54 (2 C), 1.51, 1.36, 1.34, 1.33 (2 C), 1.32 (8*s*, 5 Me_2C); 1.23–1.08 (*m*, 5 $(Me_2CH)_3Si$); 0.94 (*t*, $J = 7.5$, $(MeCH_2)_3Si$); 0.55 (*q*, $J = 7.5$, $(MeCH_2)_3Si$). HR-MALDI-MS (DHB): 2450.184 ($[M + Na]^+$, $C_{121}H_{186}Si_6N_{10}NaO_{30}^+$; calc. 2450.185).

1-[6,7-Dideoxy-2,3-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_3$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**11**). A soln. of **10** (60 mg, 25 μmol) in MeOH/AcOEt 1:1 (15 ml) was treated dropwise with a soln. of $AgNO_3$ (250 mg, 1.5 mmol) in H_2O/MeOH 1:1 (1 ml), stirred at 23° under exclusion of light for 5 h, treated with a soln.

Table 9. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Pentamers* **10**, **11**, *and* **14** *in $CDCl_3$*

	10	**11**	**14**
H–C(5/I)	5.75	5.72	5.75
H–C(5/II–V)	6.18 (2 H), 6.01 (2 H)	6.12, 6,00 (2 H), 5.98	6.17, 6.14, 6.02, 6.01
H–C(6/I)	7.27	7.23	7.24
H–C(1′/I)	5.62	5.60	5.57
H–C(1′/II–V)	6.22, 6.20, 6.19, 6.16	6.21 (3 H), 6.15	6.23, 6.22 (2 H), 6.17
H–C(2′/I–V)	5.24–4.96	5.26–4.95	5.24–4.95
H–C(3′/I–V)	5.06–4.96	5.08–4.95	5.08–4.95, 4.85[a])
H–C(4′/I)	4.19	4.21	4.19
H–C(4′/II–V)	4.13–4.03, 4.00[b])	4.13–4.02, 4.07[b])	4.14–4.03
H–C(5′/I–IV)	5.06, 5.03, 5.02, 4.99	5.08–4.95	5.08–4.95
H–C(5′/V)	4.64	4.62	3.86 (2 H)
J(1′,2′/I–V)	*ca.* 1	*ca.* 1	*ca.* 1
J(2′,3′/I–V)	[c])	[c])	[c])
J(3′,4′/I–IV)	[c])	[c])	[c])
J(3′,4′/V)	3.8	4.7	[c])
J(4′,5′/I–IV)	5.0	[c])	[c])
J(4′,5′/V)	8.0	8.3	6.2

[a]) H–C(3′/V). [b]) H–C(4′/V). [c]) Not assigned.

of KCN (241 mg, 3.6 mmol) in H_2O (1 ml), and stirred for 3 h. After evaporation, a soln. of the residue in AcOEt was washed with brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:1 → 2:1) and prep. TLC (AcOEt/hexane 1:1) gave **11** (30 mg, 52%). Yellow foam. R_f (AcOEt/hexane 1:1) 0.22. $[\alpha]_D^{25} = 2.3$ ($c = 0.4$, CH_2Cl_2). IR (CH_2Cl_2): 3374*w* (br.), 3302*w*, 3192*w*, 2946*m*, 2868*m*, 2235*w*, 1699*s*, 1596*w*, 1456*m*, 1384*m*, 1090*s*. ^{1}H-NMR (400 MHz, $CDCl_3$) see *Table 9*; additionally, 9.90, 9.62, 9.45 (2 H), 9.30 (4 br. *s*, 5 NH); 2.40 (*d*, $J = 2.2$, H–C(7′/V)); 1.57–1.52, 1.36–1.32 (several *s*, 5 Me_2C); 1.21–1.08 (*m*, 5 $(Me_2CH)_3Si$). HR-MALDI-MS (DHB): 2336.097 ($[M+Na]^+$, $C_{115}H_{172}N_{10}NaO_{30}^+$; calc. 2336.098).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**12**). A soln. of **5** (50 mg, 54 μmol), **3** [4] (35 mg, 67 μmol), $[Pd_2(dba)_3]$ (5 mg, 5.4 μmol), CuI (2 mg, 10 μmol), and $P(fur)_3$ (2.5 mg, 10 μmol) in degassed Et_3N/toluene 1:1 (5 ml) was stirred for 40 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 1:1) gave **12** (42 mg, 57%). Yellow foam. R_f (AcOEt/hexane 1:1) 0.19. $[\alpha]_D^{25} = +2.5$ ($c = 1.0$, $CHCl_3$). UV (MeOH): 286 (19400). IR ($CHCl_3$): 3386*m* (br.), 3192*w* (br.), 2945*m*, 2868*m*, 2220*w*, 1697*s*, 1596*m,* 1455*m*, 1384*m*, 1090*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 5*; additionally, 10.10, 9.92, 9.65 (3 br. *s*, 3 NH); 1.57, 1.56, 1.53, 1.37, 1.34 (6 H) (5*s*, 3 Me_2C); 1.21–1.10 (*m*, 3 $(Me_2CH)_3Si$; 1.09–1.01 (*m*, 3 $(Me_2CH)_3Si$). ^{13}C-NMR (125 MHz, $CDCl_3$): see *Table 6*; additionally, 114.8, 114.0, 113.4 (3*s*, 3 Me_2C); 27.3, 27.21, 27.19, 25.43, 25.36, 25.1 (6*q*, 3 Me_2C); 17.98 (6 C), 17.97, 17.95, 17.92, 17.90 (5*q*, 3 $(Me_2CH)_3Si$); 12.34, 12.31, 12.0 (3*d*, 3 $(Me_2CH)_3Si$). HR-MALDI-MS (DHB): 1387.661 ($[M+Na]^+$, $C_{67}H_{104}Si_3N_6NaO_{18}^+$; calc. 1387.660).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_2$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**13**). a) *From* **7** *and* **3**. A soln. of **7** (120 mg, 89 μmol), **3** (151 mg, 270 μmol), $Pd_2(dba)_3$ (34 mg, 34 μmol), CuI (14 mg, 71 μmol), and $P(fur)_3$ (16 mg, 69 μmol) in degassed Et_3N/toluene 1:1 (25 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 2:1) gave **13** (40 mg, 25%).

b) *From* **5** *and* **23**. A soln. of **5** (30 mg, 33 μmol), **23** (49 mg, 48 μmol), $[Pd_2(dba)_3]$ (6.3 mg, 6.6 μmol), CuI (1.9 mg, 10 μmol), and $P(fur)_3$ (2.3 mg, 10 μmol) in degassed Et_3N/toluene 1:1 (25 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 2:1) and prep. TLC (AcOEt/hexane 1:1) gave **13** (30 mg, 51%). Yellow foam. R_f (AcOEt/hexane 3:1) 0.44. $[\alpha]_D^{25} = +5.5$ ($c = 1.6$, $CHCl_3$). UV (MeOH): 285 (29800). IR ($CHCl_3$): 3375*m* (br.), 3192*w* (br.), 2945*m*, 2868*m*, 2235*w*, 1699*s*, 1596*m*, 1457*m*, 1384*m*, 1090*m*. ^{1}H-NMR

(500 MHz, $CDCl_3$): see *Table 7*; additionally, 10.50, 10.20, 10.0, 9.70 (4 br. *s*, 4 NH); 1.56, 1.55, 1.54, 1.52, 1.36, 1.35, 1.32, 1.31, (8*s*, 4 Me_2C); 1.21 – 1.15 (*m*, 3 (Me_2CH)$_3$Si); 1.13 – 1.10 (*m*, 3 (Me_2CH)$_3$Si; 1.09 – 1.05 (*m*, (Me_2CH)$_3$Si); 1.04 – 1.01 (*m*, (Me_2CH)$_3$Si). ^{13}C-NMR (125 MHz, $CDCl_3$): see *Table 8*; additionally, 114.7, 114.0 (2 C), 113.3 (3*s*, 4 Me_2C); 27.4 (2 C), 27.22, 27.19, 25.46, 25.36 (2 C), 25.1 (6*q*, 4 Me_2C); 18.03, 18.00, 17.99 (6 C), 17.96 (6 C), 17.92, 17.89 (6*q*, 4 (Me_2CH)$_3$Si); 12.33, 12.28 (6 C), 12.0 (3*d*, 4 (Me_2CH)$_3$Si). HR-MALDI-MS (DHB): 1849.880 ($[M+Na]^+$, $C_{90}H_{138}N_8NaO_{24}Si_4^+$; calc. 1849.880).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_3$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**14**). a) *From* **9** *and* **3**. A soln. of **9** (35 mg, 19 μmol), **3** (27 mg, 47 μmol), [Pd_2(dba)$_3$] (7.2 mg, 7.6 μmol), CuI (2.2 mg, 11 μmol), and P(fur)$_3$ (2.6 mg, 10 μmol) in degassed Et_3N/toluene 1:1 (3 ml) was stirred for 125 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 2:1) and prep. TLC gave **14** (4.6 mg, 11%).

b) *From* **7** *and* **23**. A soln. of **7** (25 mg, 18 μmol), **23** (37 mg, 36 μmol), [Pd_2(dba)$_3$] (6.8 mg, 7.2 μmol), CuI (2.7 mg, 14 μmol), and P(fur)$_3$ (3.3 mg, 14 μmol) in degassed Et_3N/toluene 1:1 (5 ml) was stirred for 100 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 2:1) and prep. TLC (AcOEt/hexane 1:1) gave **14** (6 mg, 15%). Yellow foam. R_f (AcOEt/hexane 2:1) 0.47. IR (CH_2Cl_2): 3375*m* (br.), 2945*m*, 2254*w*, 1699*s*, 1596*w*, 1456*m*, 1384*m*, 1215*m*, 1158*w*, 1089*m*, 1067*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 9*; additionally, 9.85 (br. *s*, 3 NH); 9.15, 8.85 (2 br. *s*, 2 NH); 1.56 – 1.52, 1.35 – 1.31 (several *s*, 5 Me_2C); 1.21 – 1.01 (*m*, 5 (Me_2CH)$_3$Si). HR-MALDI-MS (DHB): 2312.098 ($[M+Na]^+$, $C_{113}H_{172}N_{10}NaO_{30}Si_5^+$; calc. 2312.099).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-{(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl}$_4$-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil* (**15**). A soln. of **9** (20 mg, 11 μmol), **23** (44 mg, 43 μmol), [Pd_2(dba)$_3$] (9.5 mg, 10 μmol), CuI (1.9 mg, 10 μmol), and P(fur)$_3$ (2.3 mg, 10 μmol) in degassed Et_3N/toluene 1:1 (5 ml) was stirred for 170 h at 23°. After evaporation, FC (AcOEt/hexane 1:3 → 2:1) and prep. TLC (AcOEt/hexane 1:1) gave **15** (1.5 mg, 5%). R_f (AcOEt/hexane 1:1) 0.22. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.24 (*d*, *J* = 8.0, H–C(6/I)); 6.23 – 6.14 (*m*, H–C(1′/II – VI), H–C(5/II – IV)); 6.02 – 6.00 (several *s*, H–C(5/V – VI)); 5.75 (*d*, *J* = 8.0, H–C(5/I)); 5.57 (*s*, H–C(1′/I)); 5.24 – 5.19 (*m*, H–C(2′/II – VI)); 5.08 – 4.95 (*m*, H–C(2′/I), H–C(3′/I – V), H–C(5′/I – V)); 4.85 (*t*, *J* ≈ 5, H–C(3′/VI)); 4.19 – 4.03 (*m*, H–C(4′/I – VI); 3.86 (*d*, *J* = 6.2, 2 H–C(5′/VI)); 1.56 – 1.52, 1.35 – 1.31 (several *s*, 6 Me_2C); 1.21 – 1.01 (*m*, 6 (Me_2CH)$_3$Si). MALDI-MS (indole-3-acetic acid): 2776.6 (100, $[M+Na]^+$).

1-[6,7-Dideoxy-2,3-O-*isopropylidene-7*-C-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6 → 7′*-C*)-1-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)uracil* (**18**). A soln. of **16** [4] (6.0 g, 10.9 mmol), **17** [4] (3.2 g, 10.4 mmol), [Pd_2(dba)$_3$] (494 mg, 0.52 mmol), CuI (198 mg, 1.0 mmol), and P(fur)$_3$ (241 mg, 1.0 mmol) in degassed Et_3N/toluene 1:1 (400 ml) was stirred for 15 h at 23°. After evaporation, FC (AcOEt/hexane 4:1) gave **18** (6.9 g, 91%). Brown foam. R_f (AcOEt/hexane 4:1) 0.22. $[\alpha]_D^{25} = +29.1$ (*c* = 0.85, $CHCl_3$). UV (MeOH): 280 (sh), 265 (16300). IR (KBr): 3421*m* (br.), 3200*m* (br.), 3068*w*, 2956*m*, 2235*w*, 2178*w*, 1696*s*, 1597*s*, 1458*m*, 1384*m*, 1271*w*, 1216*m*, 1158*s*, 1088*s*. ^{1}H-NMR (400 MHz, CD_3OD): see *Table 10*; additionally, 7.78 (*d*, *J* = 8.1, H–C(6/I)); 1.57, 1.53, 1.38, 1.34 (4*s*, 2 Me_2C); 0.98 (*t*, *J* = 7.5, ($MeCH_2$)$_3$Si); 0.58 (*q*, *J* = 7.5, ($MeCH_2$)$_3$Si). ^{13}C-NMR (100 MHz, CD_3OD): see *Table 11*; additionally, 115.3, 114.8 (2*s*, 2 Me_2C); 27.6, 27.5, 25.7, 25.4 (4*q*, 2 Me_2C); 7.8 (*q*, ($MeCH_2$)$_3$Si); 4.2 (*t*, ($MeCH_2$)$_3$Si). FAB-MS (NOBA): 729 (19, $[M+H]^+$), 713 (34, $[M-Me]^+$), 699 (21, $[M-Et]^+$). Anal. calc. for $C_{34}H_{44}N_4O_{12}Si$ (728.83): C 56.03, H 6.08, N 7.69; found: C 55.98, H 6.27, N 7.49.

1-[6,7-Dideoxy-2,3-O-*isopropylidene-7*-C-*(triethylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6 → 7′*-C*)-1-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)-6-iodouracil* (**19**). At −78°, a soln. of (i-Pr)$_2$NH (3.5 ml, 25 mmol, distilled from CaH_2) in THF (100 ml) was treated dropwise with 1.65M BuLi in hexane (15.0 ml, 24 mmol), stirred at −78° for 15 min and at 0° for 15 min, cooled to −78°, treated dropwise with a soln. of **18** (1.5 g, 2.1 mmol) in THF (150 ml), stirred for 3 h, treated dropwise with NIS (5.6 g, 25 mmol) in THF (100 ml), stirred for 2 h, treated with AcOH (3 ml), and allowed to warm to 23°. After evaporation, a soln. of the residue in AcOEt was washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 2:1) gave **19** (714 mg, 40%) and **18** (325 mg, 22%).

Data of **19**: Red foam. R_f (AcOEt/hexane 3:1) 0.45. $[\alpha]_D^{25} = -52.2$ (*c* = 0.6, $CHCl_3$). UV (MeOH): 276 (16000). IR ($CHCl_3$): 3391*m* (br.), 3008*w*, 2957*w*, 2876*w*, 2225*w*, 2175*w*, 1698*s*, 1600*w*, 1385*w*, 1341*m*, 1157*w*, 1086*m*. ^{1}H-NMR (400 MHz, CD_3OD): see *Table 10*; additionally, 1.57, 1.55, 1.36, 1.35 (4*s*, 2 Me_2C); 0.98 (*t*, *J* = 7.5, ($MeCH_2$)$_3$Si); 0.59 (*q*, *J* = 7.5, ($MeCH_2$)$_3$Si). ^{13}C-NMR (100 MHz, CD_3OD): see *Table 11*; additionally, 115.0, 114.9 (2*s*, 2 Me_2C); 27.8, 27.5, 25.7, 25.5 (4*q*, 2 Me_2C); 7.8 (*q*, ($MeCH_2$)$_3$Si); 5.3 (*t*, ($MeCH_2$)$_3$Si). FAB-MS (NOBA): 855 (4, $[M+H]^+$).

Table 10. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Dimers* **4**, **5**, **20**, **22**, *and* **23** *in $CDCl_3$, and of* **18** *and* **19** *in CD_3OD* (assignment based on selective homodecoupling experiments)

	4 [4]	**5** [4]	**18**	**19**	**20**	**22**	**23**
H–C(5/I)	5.72	5.72	5.69	6.40	6.44	6.51	6.44
H–C(1′/I)	5.83	5.73	5.95	6.22	6.08	6.11	6.08
H–C(2′/I)	4.91	4.97	5.00	5.29	5.24	5.23	5.23
H–C(3′/I)	4.99	4.99	5.03	5.06	5.05	5.14	5.00
H–C(4′/I)	4.22	4.22	4.28	4.13	4.16	4.28	4.15
H–C(5′/I)	5.04	5.03	4.86	4.77	4.99	4.87	4.99
J(1′,2′/I)	2.4	1.9	2.4	1.4	1.5	2.0	1.5
J(2′,3′/I)	6.6	6.6	6.4	6.4	6.5	6.5	6.3
J(3′,4′/I)	4.3	3.6	3.0	3.7	4.2	4.1	4.4
J(4′,5′/I)	4.6	5.5	5.3	8.5	6.8	5.6	6.5
H–C(5/II)	5.97	5.93	5.98	5.96	6.04	6.04	6.03
H–C(1′/II)	6.14	6.21	6.24	6.30	6.21	6.24	6.24
H–C(2′/II)	5.24	5.19	5.33	5.32	5.24	5.21	5.20
H–C(3′/II)	5.05	5.04	5.00	5.01	5.00	4.85	4.84
H–C(4′/II)	4.01	4.04	4.00	4.07	4.03	4.21	4.15
H–C(5′/II)	4.64	4.64	4.56	4.56	4.65	3.87 (2 H)	3.85 (2 H)
J(1′,2′/II)	1.2	1.5	2.0	2.3	1.5	1.4	1.1
J(2′,3′/II)	6.5	6.6	6.5	6.5	6.5	6.5	6.4
J(3′,4′/II)	3.6	3.6	3.2	3.1	3.8	4.3	4.5
J(4′,5′/II)	8.1	8.6	7.6	7.5	8.0	6.4	6.4

Table 11. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Dimers* **4**, **5**, **20**, **22**, *and* **23** *in $CDCl_3$, and* of **18** *and* **19** *in CD_3OD Solution*

	4 [4][a])	**5** [4]	**18**	**19**	**20**	**22**	**23**
C(2/I)	163.3	162.9	166.1	164.8	162.3	162.8	162.9
C(4/I)	150.0	149.8	152.0	151.8	149.3	149.6	149.6
C(5/I)	102.7	102.8	102.8	117.4	117.0	117.5	117.0
C(6/I)	141.6	142.2	144.0	116.3	114.1	117.5	117.0
C(1′/I)	93.0	94.2	96.0	103.7	102.1	102.1	101.9
C(2′/I)	84.0	84.0	85.7	85.9	83.9	84.1	84.3
C(3′/I)	80.0	80.7	83.9	84.2	82.6	82.2	82.3
C(4′/I)	88.5	89.0	91.6	91.9	91.0	89.5	90.0
C(5′/I)	63.6	63.7	63.8	63.9	64.3	62.9	64.3
C(6′/I)	100.4	101.0	102.2	103.5	101.8	100.7	101.7
C(7′/I)	76.7	76.6	76.9	76.1	75.8	76.2	75.8
C(2/II)	162.4	161.9	164.5	163.8	161.1	161.3	161.5
C(4/II)	149.4	149.3	151.7	149.4	147.1	148.1	147.1
C(5/II)	108.5	108.3	109.3	108.8	108.1	108.4	107.9
C(6/II)	137.6	137.5	138.8	139.1	138.0	137.7	138.0
C(1′/II)	94.6	94.7	95.0	96.3	94.4	94.1	94.0
C(2′/II)	83.8	83.9	84.8	84.7	83.8	83.6	83.9
C(3′/II)	82.7	82.7	82.4	84.0	82.4	80.9	82.1
C(4′/II)	91.2	91.3	89.7	91.4	90.2	89.1	89.7
C(5′/II)	63.8	63.3	63.5	63.7	63.8	64.3	64.4
C(6′/II)	106.3	83.8	107.3	107.3	106.4	–	–
C(7′/II)	87.8	73.7	88.2	88.3	87.8	–	–

[a]) Assignment based on a HSQC.GRASP spectrum.

1-[6,7-Dideoxy-2,3-O-*isopropylidene-7*-C-*(triethylsilyl)-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]uracil-6-yl-(6 → 7′*-C*)-1-[6,7-dideoxy-2,3*-O-*isopropylidene-5*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl]-6-iodouracil* (**20**). A soln. of 2,6-di(*tert*-butyl)pyridine (1.6 ml, 8.4 mmol) and **19** (500 mg, 0.7 mmol) in CH_2Cl_2 (30 ml) was treated dropwise with TIPSOTf (0.76 ml, 3.1 mmol), stirred at 23° for 20 min, washed with brine (2 × 10 ml), dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 2:5) gave **20** (423 mg, 62%). Colourless powder. R_f (AcOEt/hexane 1:1) 0.58. $[\alpha]_D^{25} = +7.9$ ($c = 1.7$, $CHCl_3$). UV (MeOH): 276 (15000). IR ($CHCl_3$): 3385*w*, 2946*m*, 2868*m*, 2225*w*, 2175*w*, 1695*s*, 1595*w*, 1577*w*, 1384*m*, 1339*w*, 1265*w*, 1092*m*, 1068*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 10*, additionally, 9.55, 8.85 (2 br. *s*, 2 NH); 1.57, 1.55, 1.35, 1.33 (4*s*, 2 Me_2C); 1.23–1.15 (*m*, 2 $(Me_2CH)_3Si$); 1.13–1.08 (*m*, 2 $(Me_2CH)_3Si$; 0.94 (*t*, $J = 7.5$, $(MeCH_2)_3Si$); 0.55 (*q*, $J = 7.5$, $(MeCH_2)_3Si$). ^{13}C-NMR (100 MHz, $CDCl_3$): see *Table 11*; additionally, 113.5, 113.4 (2*s*, 2 Me_2C); 27.2, 27.1, 25.2, 25.1 (4*q*, 2 Me_2C); 18.09, 18.06, 18.00 (6 C) (3*q*, 2 $(Me_2CH)_3Si$); 12.5, 12.3 (2*d*, 2 $(Me_2CH)_3Si$); 7.3 (*q*, $(MeCH_2)_3Si$); 4.2 (*t*, $(MeCH_2)_3Si$). MALDI-MS (indole-3-acetic acid): 1191 (100, $[M + Na]^+$), 1207 (25, $[M + K]^+$). Anal. calc. for $C_{52}H_{83}IN_4O_{12}Si_3$ (1167.41): C 53.50, H 7.17, N 4.80; found: C 53.37, H 7.00, N 4.80.

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-(6 → 7′*-C*)-1-(6,7-dideoxy-2,3*-O-*isopropylidene-β*-D-allo-*hept-6-ynofuranosyl)-6-iodouracil* (**22**). At −78°, a soln. of $(i\text{-}Pr)_2NH$ (3.4 ml, 24 mmol, distilled from CaH_2) in THF (50 ml) was treated dropwise with 1.65M BuLi in hexane (14.5 ml, 24 mmol), stirred at −78° for 15 min and at 0° for 15 min, cooled to −78°, treated dropwise with a soln. of **21** [4] (1.5 g, 2 mmol) in THF (80 ml), stirred for 2.5 h, treated dropwise with NIS (5.4 g, 24 mmol) in THF (100 ml), stirred for 1.5 h, treated with AcOH (1 ml), and allowed to warm to 23°. After evaporation, a soln. of the residue in AcOEt was washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 2:1) gave **22** (707 mg, 40%) and **21** (300 mg, 20%).

Data of **22**. Red foam. R_f (AcOEt/hexane 3:1) 0.59. $[\alpha]_D^{25} = +16.7$ ($c = 0.7$, $CHCl_3$). UV (MeOH): 276 (16800). IR ($CHCl_3$): 3390*w* (br.), 3008*w*, 2944*w*, 2867*w*, 2220*w*, 1721*s*, 1697*s*, 1596*w*, 1433*w*, 1385*m*, 1341*w*, 1158*m*, 1087*m*, 1069*m*, 882*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 10*; additionally, 10.40, 9.70 (2 br. *s*, 2 NH); 1.60, 1.56, 1.37, 1.34 (4*s*, 2 Me_2C); 1.08–1.03 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (100 MHz, $CDCl_3$): see *Table 11*; additionally, 113.8, 113.3 (2*s*, 2 Me_2C); 27.3, 27.1, 25.5, 25.3 (4*q*, 2 Me_2C); 17.93, 17.90 (2*q*, $(Me_2CH)_3Si$); 11.9 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 874 (80, $[M + H]^+$), 858 (44, $[M - Me]^+$), 829 (100, $[M - Me_2C]^+$).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridin-6-yl-(6 → 7′*-C*)-1-(6,7-dideoxy-2,3*-O-*isopropylidene-5′*-O-*(triisopropylsilyl)-β*-D-allo-*hept-6-ynofuranosyl)-6-iodouracil* (**23**). A soln. of 2,6-di(*tert*-butyl)pyridine (0.45 ml, 2 mmol) and **22** (150 mg, 0.17 mmol) in CH_2Cl_2 (10 ml) was treated dropwise with TIPSOTf (0.18 ml, 0.69 mmol), stirred at 23° for 30 min, washed with brine (2 × 10 ml), dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1:2) gave **23** (88 mg, 50%). Colourless powder. R_f (AcOEt/hexane 1:1) 0.36. $[\alpha]_D^{25} = -3.4$ ($c = 1.2$, $CHCl_3$). UV (MeOH): 272 (15500). IR ($CHCl_3$): 3384*w*, 2945*w*, 2867*w*, 2220*w*, 1695*s*, 1595*w*, 1455*m*, 1384*m*, 1148*w*, 1089*m*, 1068*m*, 882*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 10*; additionally, 10.00, 9.50 (2 br. *s*, 2 NH); 1.57, 1.55, 1.35, 1.34 (4*s*, 2 Me_2C); 1.13–1.10 (*m*, $(Me_2CH)_3Si$); 1.07–1.02 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (100 MHz, $CDCl_3$): see *Table 11*; additionally, 113.6, 113.5 (2*s*, 2 Me_2C); 27.3, 27.2, 25.4, 25.3 (4*q*, 2 Me_2C); 17.95, 17.92 (2*q*, 2 $(Me_2CH)_3Si$); 12.3, 11.9 (2*d*, 2 $(Me_2CH)_3Si$). MALDI-MS (indole-3-acetic acid): 1051 (100, $[M + Na]^+$), 1067 (20, $[M + K]^+$). Anal. calc. for $C_{44}H_{69}IN_4O_{12}Si_2$ (1029.12): C 51.35, H 6.76, N 5.44; found: C 51.33, H 6.72, N 5.32.

Uridin-6-yl-(6 → 7′-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil-6-yl-(6 → 7′*-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil* (**24**). A soln. of **12** (20 mg, 14.6 μmol) in MeCN/H_2O/40% HF/37% HCl 100:50:2:2 (3 ml) was stirred at 40° for 100 h. Evaporation and HPLC (H_2O/MeOH 10:0 → 1:9) gave **24** (8 mg, 70%). White powder. $[\alpha]_D^{25} = +2.1$ ($c = 0.53$, H_2O). UV (MeOH): 276 (18300). IR (KBr): 3396*s* (br.), 2237*w*, 1686*s*, 1598*m*, 1460*m*, 1390*s*, 1267*w*, 1226*w*, 1109*m*, 1054*m*, 830*w*, 765*w*. ^{1}H-NMR (400 MHz, D_2O): see *Table 12*. ^{13}C-NMR (100 MHz, D_2O): see *Table 6*. ESI-MS (pos. ions): 799 (100, $[M + Na]^+$), 777 (10, $[M + H]^+$). ESI-MS (neg. ions): 811.3 (35, $[M + Cl]^-$), (100, $[M - H]^-$).

Uridin-6-yl-[(6 → 7′-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil-6-yl]$_2$-(6 → 7′*-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil* (**25**). A soln. of **13** (20 mg, 11 μmol) in MeCN/H_2O/40% HF/37% HCl 100:50:2:2 (3 ml) was stirred at 40° for 125 h. Evaporation and HPLC (H_2O/MeOH 10:0 → 1:9) gave **25** (7.6 mg, 67%). White powder. $[\alpha]_D^{25} = +9.7$ ($c = 0.35$, H_2O). UV (MeOH): 283 (27400). IR (KBr): 3410*s* (br.), 2238*w*, 1686*s*, 1597*m*, 1458*w*, 1388*m*, 1113*m*, 1053*m*. ^{1}H-NMR (500 MHz, D_2O) see *Table 12*. ^{13}C-NMR (125 MHz, D_2O): see *Table 8*. MALDI-MS (CCA): 1065.2 (100, $[M + Na]^+$), 1081.4 (13, $[M + K]^+$). ESI-MS (pos. ions): 1065.4 (60, $[M + Na]^+$), 1043.4 (10, $[M + H]^+$). ESI-MS (neg. ions): 1077.4 (30, $[M + Cl]^-$); 1041.4 (100, $[M - H]^-$).

Uridin-6-yl-[(6 → 7′-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil-6-yl]$_3$-(6 → 7′*-C*)-1-(6,7-dideoxy-β*-D-allo-*hept-6-ynofuranosyl)uracil* (**26**). A soln. of **14** (3 mg, 1.3 μmol) in MeCN/H_2O/40% HF/37%

Table 12. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Deprotected Trimer* **24**, *Tetramer* **25**, *and Pentamer* **26** *in D_2O*

	24	**25**	**26**
H–C(5/I)	5.86	5.79	5.86
H–C(5/II–V)	6.17, 6.15	6.10 (2 H), 6.08	6.17 (2 H), 6.16 (2 H)
H–C(6/I)	7.80	7.74	7.79
H–C(1′/I)	5.93	5.86	5.92
H–C(1′/II–V)	6.13, 6.08	6.07, 6.06, 6.00	6.15, 6.14 (2 H), 6.07
H–C(2′/I)	4.41	4.46	4.54–4.50
H–C(2′/II–V)	4.93, 4.76	4.88–4.82 (2 H), 4.69[a])	4.94–4.89 (3 H), 4.73[b])
H–C(3′/I–V)	4.37, 4.42, 4.54	4.29 (2 H), 4.35 (2 H)	4.54–4.50 (2 H), 4.42–4.41 (2 H), 4.36
H–C(4′/I–V)	4.25, 4.02, 3.89	4.18, 3.96, 3.92, 3.81	4.25, 4.02, 3.97, 3.96, 3.89
H–C(5′/I–V)	4.97, 4.95, 3.82/3.72	4.91, 4.88–4.82 (2 H), 3.76–3.64	4.98, 4.93, 4.90, 4.89, 3.82/3.71
J(1′,2′/I)	4.8	4.5	4.7
J(1′,2′/II–V)	4.1, 3.6	[c]), 3.6, 4.5	6.0, 4.2, 4.2, 3.7
J(2′,3′/I–V)	5.5, 6.1, 6.4	5.7, [c]), [c]), 6.6	[c]), [c]), [c]), [c]), 6.5
J(3′,4′/I–V)	4.0, 5.7, 3.2	3.6, 5.8, 5.8, 3.0	4.0, 5.9, 5.6, 5,9, 3.0
J(4′,5′/I–II)	4.2, 5.6	4.2, 5.8	6.2, 5.6
J(4′,5′/III)	3.3, 6.1	5.8	5.9
J(4′,5′/IV)	–	3.0, 5.9	6.8
J(4′,5′/V)	–	–	3.2, 5.9

[a]) H–C(2′/IV). [b]) H–C(2′/V). [c]) Not assigned.

HCl 100:50:2:2 (1 ml) was stirred at 40° for 150 h. Evaporation and HPLC (H_2O/MeOH 10:0 → 1:9) gave **26** (1.0 mg, 58%). White powder. UV (MeOH): 282 (37800). ^{1}H-NMR (500 MHz, D_2O): see *Table 12*. MALDI-MS (CCA): 1331.8 (100, $[M+Na]^+$), 1348.2 (20, $[M+K]^+$).

Synthesis of the rA_5, rA_7, rU_5, and rU_7 Oligomers. The solid-phase syntheses were carried out on a *Pharmacia* gene-assembler on a 1.3-μmol scale according to the protocol developed by *Pitsch et al.* [15]. The commercial phosphoamidites and the CPG solid supports were obtained from *Xeragon*. The removal of the base- and phosphate-protecting groups and the cleavage from the solid support was accomplished with a 1:1 mixture of $MeNH_2$ (40% in H_2O) and $MeNH_2$ (30% in EtOH), while the $(i\text{-}Pr)_3SiOCH_2$ groups at O(2′) were cleaved with 1M Bu_4NF in THF. The crude products were desalted on a *Sephadex* column, and purified or completely desalted by RP-HPLC. The composition of the oligonucleotides was evidenced by MALDI-TOF-MS (*cf. Table 4*).

Measurement of Hyperchromicities. A Cary 3E UV/VIS spectrophotometer (*Varian*) equipped with *Cary* temp. controller, sample transport accessory, multi cell block, and *Hellma* cuvettes (size: *ca.* 1 ml, inner diameter: 4 mm, path of rays: 10 mm) was used. The temp. was measured with a reference cuvette (temp. gradient: 0.5°/min). The spectrometer was flushed with N_2, and the solns. (15 μmol solns. of the nucleosides in a 10-mmol NaH_2PO_4/Na_2HPO_4 buffer at pH 7 and at a 0.2M concentration of NaCl) in the cuvettes were overlaid with dimethylpolysiloxane.

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