

Oligonucleosides with a Nucleobase-Including Backbone

Part 11

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

by Simon Eppacher, Nathalie Solladié, and Andrea Vasella*

Laboratorium für Organische Chemie, ETH Hönggerberg, HCI CH-8093 Zürich

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 rA₇, nor for the pairing of rU₅ and rA₇, while a UV melting experiment showed the beginning of a sigmoid curve for the interaction of rU₇ with rA₇. Therefore, the pentamer **26** does not pair more strongly with rA₇ than rU₅.

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 CHCl₃ 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*).

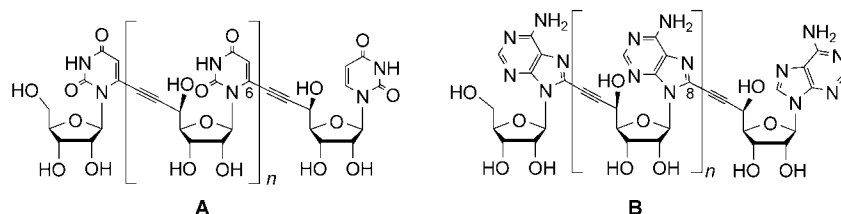


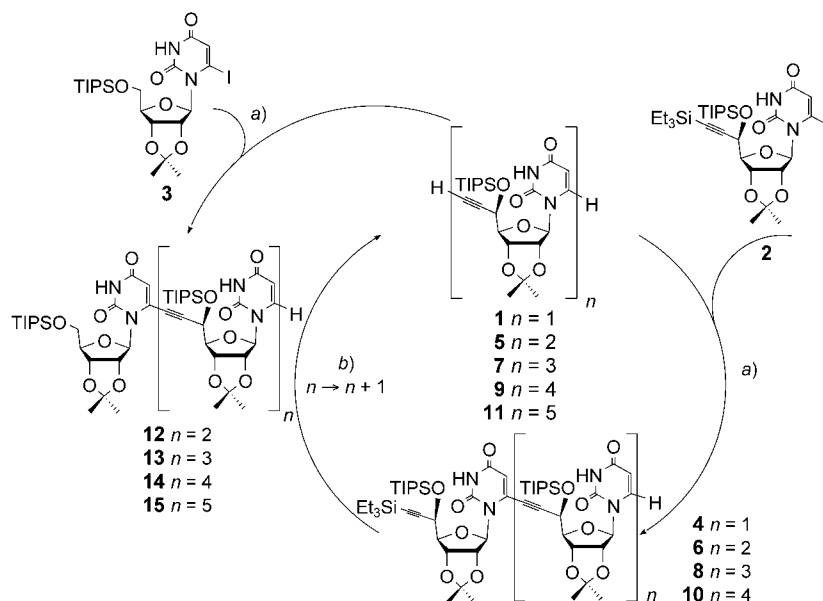
Fig. 1. Uridine- and adenosine-derived ethynylene-linked oligonucleosides **A** and **B**

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% $[\text{Pd}_2(\text{dba})_3]$, 7% CuI and 7% $\text{P}(\text{fur})_3$ to yield 77% of the dimer **4** [4] (*Scheme 1*). C-Desilylation of **4** led in 63% yield¹⁾ 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 $\text{P}(\text{fur})_3$ by $\text{P}(\text{i-Pr})_3$ or $\text{Ph}_2\text{P}(\text{CH}_2)_n\text{PPh}_2$ ($n = 2, 3$, 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 $[\text{Pd}_2(\text{dba})_3]$ and 1 equiv. each of CuI and $\text{P}(\text{fur})_3$ 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

- 1) When the HO–C(5') groups were protected as Et_3Si -ethers instead of $(\text{i-Pr})_3\text{Si}$ (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) $[\text{Pd}_2(\text{dba})_3]$ (dba = dibenzylideneacetone = 1,5-diphenylpenta-1,4-dien-3-one), CuI, $\text{P}(\text{fur})_3$, 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 $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PX}_3$	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) $\text{PX}_3 = \text{Ph}_2\text{P}(\text{CH}_2)_n\text{PPh}_2$ ($n = 2, 3$, 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.

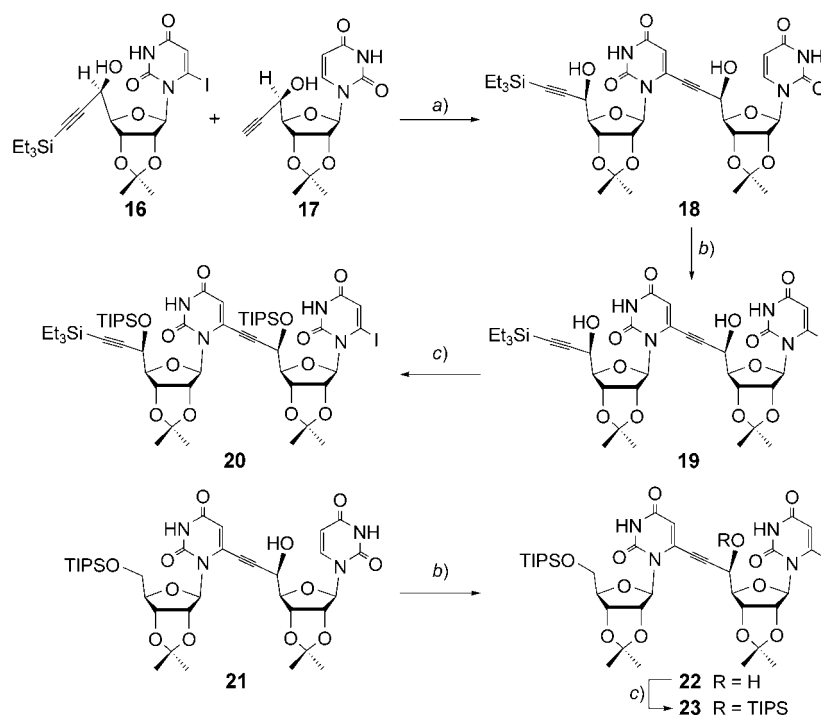
To reduce the number of coupling steps and to alleviate the separation problem, we also investigated a convergent approach, *i.e.*, coupling of the iodinated dimers **20** and **23** (Scheme 2) with the dimer **5**, trimer **7**, and tetramer **9** (Scheme 3). Coupling of the alkyne **17** [4] with the 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**

	<i>n</i>	[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.

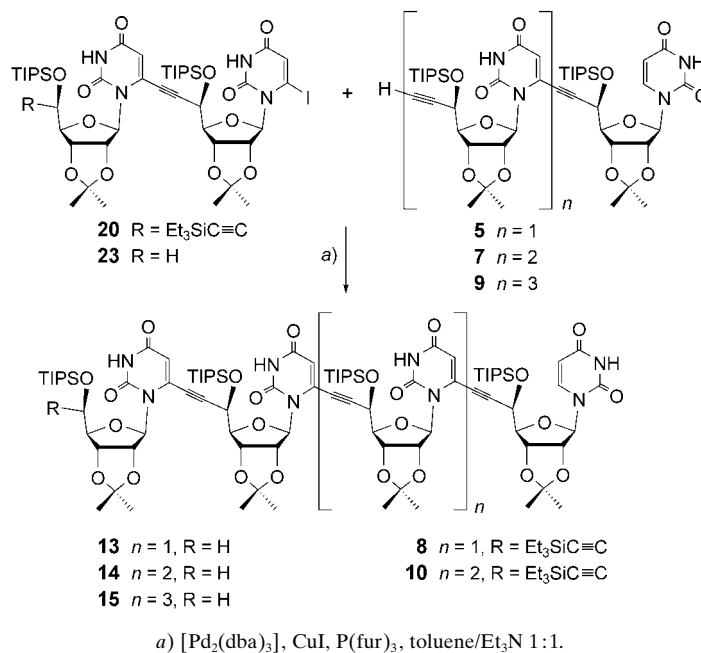
Scheme 2



a) [Pd₂(dba)₃], CuI, P(fur)₃, toluene/Et₃N 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, CH₂Cl₂; 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-tetramethylpiperide

Scheme 3



(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 CH₂Cl₂ 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.

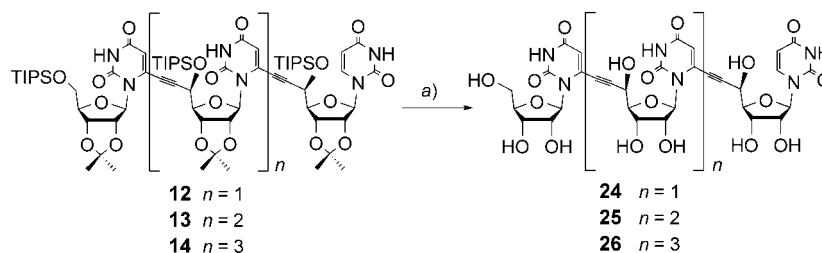
Table 3. Conditions and Yields of the Cross-Coupling of the Dimeric Iodides **20** and **23** with the Acetylenes **5**, **7**, and **9**

	<i>n</i>	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 H₂O/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



a) H₂O/MeCN/37% HCl/40% HF 100:50:2:2; 70% of **24**, 67% of **25**, 58% of **26**.

The ¹H-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 ³T₂ 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 ¹³C-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 ss for C(6') and C(7') of the $\text{C}\equiv\text{C}-\text{SiEt}_3$ groups of **4** and **18–20** appear at 106.3–107.3 and 87.8–88.2 ppm, and the ss for C(6') and C(7') of the bridging $\text{C}\equiv\text{C}$ 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 $J(1',2') = 0\text{--}1.9$ to $J(3',4') = 2.8\text{--}5.6$ Hz indicates a preference for the 3T_2 sugar pucker. The large $J(4',5') = 5.0\text{--}8.0$ 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 $\text{C}\equiv\text{CH}$ 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 $\text{C}\equiv\text{CSiEt}_3$ 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 $J(1',2') = 3.6\text{--}6.0$ to $J(3',4') = 3.2\text{--}5.8$ 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 ($\chi = 45\text{--}75^\circ$) is not in agreement with the χ angles of $115\text{--}145^\circ$ 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** ($\text{26} \cdot \text{rA}_5$ and $\text{26} \cdot \text{rA}_7$) as compared to RNA duplexes ($\text{rU}_5 \cdot \text{rA}_5$ and $\text{rU}_7 \cdot \text{rA}_7$) were prepared by solid-phase synthesis according to [15].

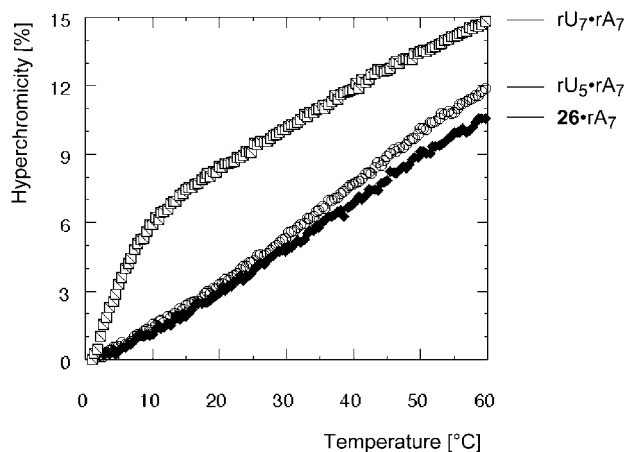
Neither the 15:15 μmol mixtures of the pentamer **26** and the RNA strand A_5 or A_7 , nor the mixtures A_5 and U_5 , nor A_7 and U_5 showed any sigmoid UV melting curve in a 10-mmol $\text{NaH}_2\text{PO}_4/\text{Na}_2\text{HPO}_4$ buffer at pH 7 and at a 0.2M concentration of NaCl (*Fig. 2*). A first indication for a sigmoid curve was only visible in the temperature-dependent UV curve of the RNA duplex $\text{rA}_7 \cdot \text{rU}_7$, indicating that the pentamer **26** does not bind to RNA more strongly than the RNA strand rU_5 .

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 rA₅, rA₇, rU₅, and rU₇*

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·(rA₇), (rU₅)·(rA₇), and (rU₇)·(rA₇)*

We thank Dr. B. Berner 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, CH₂Cl₂ from CaH₂. Reactions were run under Ar. Qual. TLC: precoated silica-gel plates (Merck silica gel 60 F₂₅₄); detection by spraying with 'mostain' (400 ml of 10% aq. H₂SO₄, 20 g of (NH₄)₆Mo₇O₂₄·H₂O, 0.4 g of Ce(SO₄)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. ¹H- and ¹³C-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), [Pd₂(dba)₃] (228 mg, 0.24 mmol), CuI (68 mg, 0.36 mmol), and P(fur)₃ (83 mg, 0.36 mmol) in degassed Et₃N/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. [α]_D²⁵ = +7.6 (c = 0.8, CHCl₃). IR (CHCl₃): 3373m (br.), 3192m (br.), 2949m, 2869w, 2233w, 2178w, 1699s, 1597w, 1455m, 1382m, 1216m, 1091s. ¹H-NMR (500 MHz, CDCl₃): 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 (6s, 3 Me₂C); 1.23–1.15 (*m*, 3 (Me₂CH)₃Si); 1.13–1.08 (*m*, 3 (Me₂CH)₃Si); 0.93 (*t*, *J* = 7.8, (MeCH₂)₃Si); 0.55 (*q*, *J* = 7.8, (MeCH₂)₃Si). ¹³C-NMR (125 MHz, CDCl₃): see Table 6, additionally, 114.8, 113.9, 113.3 (3s, 3 Me₂C); 27.22, 27.20, 27.1, 25.4, 25.1, 25.0 (6*q*, 3 Me₂C); 18.10, 18.08, 18.0 (6 C), 17.97, 17.96 (5*q*, 3 (Me₂CH)₃Si); 12.5, 12.4, 12.3 (3*d*, 3 (Me₂CH)₃Si); 7.3 (*q*, (MeCH₂)₃Si); 4.2 (*t*, (MeCH₂)₃Si). HR-MALDI-MS (DHB): 1525.748 ([*M* + Na]⁺, C₇₅H₁₁₈Si₄N₆NaO₁₈; calc. 1525.748).

Table 5. Selected ¹H-NMR Chemical Shifts [ppm] and Coupling Constants [Hz] of the Trimers **6**, **7**, and **12** in CDCl₃ (assignment based on selective homodecoupling experiments)

	6	7	12		6	7	12
H–C(5/I)	5.72	5.72	5.73	<i>J</i> (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	<i>J</i> (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	<i>J</i> (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	<i>J</i> (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	<i>J</i> (3',4'/II)	4.5	4.5	4.6
H–C(3'/III)	5.05	5.07–4.96	4.85	<i>J</i> (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	<i>J</i> (4',5'/I)	5.2	5.6	8.0
H–C(4'/III)	4.01	4.05	4.14	<i>J</i> (4',5'/II)	6.5	6.5	8.0
H–C(5'/I)	5.06	5.06	5.06	<i>J</i> (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 ¹³C-NMR Chemical Shifts [ppm] of the Trimers **6**, **7**, and **12** in CDCl₃, and of **24** in D₂O 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 AgNO₃ (2.4 g, 49.5 mmol) in H₂O/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 H₂O (10 ml), and stirred for 1 h. After evaporation, a soln. of the residue in AcOEt was washed with brine, dried (Na₂SO₄), 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): 3372w (br.), 3301w, 2947m, 2868m, 2233w, 1700s, 1597w, 1454m, 1381m, 1091s. $^1\text{H-NMR}$ (400 MHz, CDCl_3): see Table 5; additionally, 9.90, 9.48 (2 H) (2 br. s, 3 NH); 2.40 (d , $J = 2.0$, $\text{H-C}(7'/\text{III})$); 1.57, 1.55, 1.51, 1.36, 1.33, 1.32 (6s, 3 Me_2C); 1.23–1.08 (m , 3 (Me_2CH) $_3\text{Si}$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): see Table 6; additionally, 114.8, 113.9, 113.3 (3s, 3 Me_2C); 27.23, 27.21, 27.1, 25.4, 25.1, 25.0 (6q, 3 Me_2C); 18.10 (6 C), 18.08, 18.00, 17.97, 17.96 (5q, 3 (Me_2CH) $_3\text{Si}$); 12.5, 12.4, 12.3 (3d, 3 (Me_2CH) $_3\text{Si}$). HR-MALDI-MS (DHB): 1141.660 ($[M + \text{Na}]^+$, $\text{C}_{69}\text{H}_{104}\text{N}_6\text{NaO}_{18}\text{Si}_3^+$; 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 $\rightarrow$ 7'-C)-1-[6,7-dideoxy-2,3-O-isopropylidene-5-O-(triisopropylsilyl)- β -D-allo-hept-6-ynofuranosyl]uracil-6-yl] $_2$ -(6 $\rightarrow$ 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), $[\text{Pd}_2(\text{dba})_3]$ (41.3 mg, 43 μmol), CuI (16 mg, 86 μmol), and $\text{P}(\text{fur})_3$ (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 $\rightarrow$ 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), $[\text{Pd}_2(\text{dba})_3]$ (6.3 mg, 6.4 μmol), CuI (1.8 mg, 9.4 μmol), and $\text{P}(\text{fur})_3$ (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 $\rightarrow$ 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): 3375m (br.), 3192w (br.), 2949m, 2868m, 2235w, 1699s, 1596w, 1456m, 1384m, 1215m, 1092s. $^1\text{H-NMR}$ (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 (8s, 4 Me_2C); 1.23–1.15 (m , 4 (Me_2CH) $_3\text{Si}$); 1.13–1.08 (m , 4 (Me_2CH) $_3\text{Si}$); 0.94 (t , $J = 7.5$, (MeCH_2) $_3\text{Si}$); 0.55 (q , $J = 7.5$, (MeCH_2) $_3\text{Si}$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): see Table 8; additionally, 114.7, 114.0, 113.9, 113.3 (4s, 4 Me_2C); 27.2 (3 C), 27.1, 25.35, 25.23, 25.07, 25.04 (6q, 4 Me_2C); 18.10, 18.08, 18.02, 17.97 (4q, 4 (Me_2CH) $_3\text{Si}$); 12.5, 12.34 (6 C), 12.30 (3d, 4 (Me_2CH) $_3\text{Si}$); 7.3 (q , (MeCH_2) $_3\text{Si}$); 4.2 (t , (MeCH_2) $_3\text{Si}$). HR-MALDI-MS (DHB): 1987.967 ($[M + \text{Na}]^+$, $\text{C}_{98}\text{H}_{152}\text{N}_8\text{NaO}_{24}\text{Si}_4^+$; calc. 1987.966).

Table 7. Selected $^1\text{H-NMR}$ 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)
$J(1',2'/\text{I})$	1.9	1.8	1.4
$J(1',2'/\text{II–IV})$	0.0, 1.1, 0.0	1.0, 1.5, 1.0	0.0, 1.2, 1.0
$J(2',3'/\text{I–IV})$	6.4, 6.4, ^b), ^b)	^b)	^b)
$J(3',4'/\text{I–IV})$	3.8, 4.0, 4.6, 3.6	4.0, 5.6, 1.7, 3.9	^b)
$J(4',5'/\text{I–III})$	5.3, 6.6, 7.2	5.3, 6.9, 4.8	^b)
$J(4',5'/\text{IV})$	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 $\rightarrow$ 7'-C)-1-[6,7-dideoxy-2,3-O-isopropylidene-5-O-(triisopropylsilyl)- β -D-allo-hept-6-ynofuranosyl]uracil-6-yl] $_2$ -(6 $\rightarrow$ 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 $\text{H}_2\text{O}/\text{MeOH}$ 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 $\rightarrow$ 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): 3372w (br.), 3301w, 3193w, 3068w, 2947m, 2868m, 2234w, 1699s, 1597w, 1455m, 1382m, 1090s. ^1H -NMR (400 MHz, CDCl_3): see Table 7; additionally, 10.05 (br. s, 2 NH); 9.42 (br. s, 2 NH); 2.41 (d , $J = 2.0$, $\text{H}-\text{C}(7'/\text{IV})$); 1.57, 1.56, 1.54, 1.52, 1.36, 1.34, 1.33, 1.32 (8s, 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 (4s, 4 Me_2C); 27.25, 27.21, 27.18, 27.11, 25.4, 25.3, 25.10, 25.08 (8q, 4 Me_2C); 18.03 (12 C), 18.00, 17.96 (3q, 4 (Me_2CH)₃Si); 12.4, 12.32 (6 C), 12.27 (3d, 4 (Me_2CH)₃Si). HR-MALDI-MS (DHB): 1873.879 ($[M + \text{Na}]^+$, $\text{C}_{92}\text{H}_{138}\text{N}_8\text{NaO}_{24}\text{Si}_4$; 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 \rightarrow 7\text{-C})\text{-}1\text{-}[6,7\text{-dideoxy-}2,3\text{-O-isopropylidene-}5\text{-O-(triisopropylsilyl)-}\beta\text{-D-allo-hept-6-ynofuranosyl]uracil-6-yl}\}_3\text{-}(6 \rightarrow 7\text{-C})\text{-}1\text{-}[6,7\text{-dideoxy-}2,3\text{-O-isopropylidene-}5\text{-O-(triisopropylsilyl)-}\beta\text{-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), $[\text{Pd}_2(\text{dba})_3]$ (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 $\rightarrow$ 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), $[\text{Pd}_2(\text{dba})_3]$ (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 $\rightarrow$ 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): 3372m (br.), 3193m (br.), 2946m, 2235w, 1699s, 1595w, 1457m, 1384m, 1214m, 1091s. ^1H -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 (8s, 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 ($[M + \text{Na}]^+$, $\text{C}_{121}\text{H}_{186}\text{Si}_6\text{N}_{10}\text{NaO}_{30}$; calc. 2450.185).

1-[6,7-Dideoxy-2,3-O-isopropylidene-5-O-(triisopropylsilyl)- β -D-allo-hept-6-ynofuranosyl]uracil-6-yl- $\{(6 \rightarrow 7\text{-C})\text{-}1\text{-}[6,7\text{-dideoxy-}2,3\text{-O-isopropylidene-}5\text{-O-(triisopropylsilyl)-}\beta\text{-D-allo-hept-6-ynofuranosyl]uracil-6-yl}\}_3\text{-}(6 \rightarrow 7\text{-C})\text{-}1\text{-}[6,7\text{-dideoxy-}2,3\text{-O-isopropylidene-}5\text{-O-(triisopropylsilyl)-}\beta\text{-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 $\text{H}_2\text{O}/\text{MeOH}$ 1 : 1 (1 ml), stirred at 23° under exclusion of light for 5 h, treated with a soln.$

Table 9. Selected ^1H -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)
$J(1',2'/\text{I–V})$	ca. 1	ca. 1	ca. 1
$J(2',3'/\text{I–V})$	^c)	^c)	^c)
$J(3',4'/\text{I–IV})$	^c)	^c)	^c)
$J(3',4'/\text{V})$	3.8	4.7	^c)
$J(4',5'/\text{I–IV})$	5.0	^c)	^c)
$J(4',5'/\text{V})$	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 $\rightarrow$ 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): 3374w (br.), 3302w, 3192w, 2946m, 2868m, 2235w, 1699s, 1596w, 1456m, 1384m, 1090s. ^1H -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 ($[M + \text{Na}]^+$, $\text{C}_{115}\text{H}_{172}\text{N}_{10}\text{NaO}_{30}$; calc. 2336.098).

2',3'-O-Isopropylidene-5'-O-(triisopropylsilyl)uridin-6-yl-(6 $\rightarrow$ 7'-C)-1-[6,7-dideoxy-2,3-O-isopropylidene-5-O-(triisopropylsilyl)- β -D-allo-hept-6-ynofuranosyl]uracil-6-yl-(6 $\rightarrow$ 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), $[\text{Pd}_2(\text{dba})_3]$ (5 mg, 5.4 μmol), CuI (2 mg, 10 μmol), and $\text{P}(\text{fur})_3$ (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 $\rightarrow$ 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): 3386m (br.), 3192w (br.), 2945m, 2868m, 2220w, 1697s, 1596m, 1455m, 1384m, 1090m. ^1H -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) (5s, 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 (3s, 3 Me_2C); 27.3, 27.21, 27.19, 25.43, 25.36, 25.1 (6q, 3 Me_2C); 17.98 (6 C), 17.97, 17.95, 17.92, 17.90 (5q, 3 (Me_2CH)₃Si); 12.34, 12.31, 12.0 (3d, 3 (Me_2CH)₃Si). HR-MALDI-MS (DHB): 1387.661 ($[M + \text{Na}]^+$, $\text{C}_{67}\text{H}_{104}\text{Si}_3\text{N}_6\text{NaO}_{18}$; calc. 1387.660).

2',3'-O-Isopropylidene-5'-O-(triisopropylsilyl)uridin-6-yl-[(6 $\rightarrow$ 7'-C)-1-[6,7-dideoxy-2,3-O-isopropylidene-5-O-(triisopropylsilyl)- β -D-allo-hept-6-ynofuranosyl]uracil-6-yl]₂-(6 $\rightarrow$ 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), $\text{Pd}_2(\text{dba})_3$ (34 mg, 34 μmol), CuI (14 mg, 71 μmol), and $\text{P}(\text{fur})_3$ (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 $\rightarrow$ 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), $[\text{Pd}_2(\text{dba})_3]$ (6.3 mg, 6.6 μmol), CuI (1.9 mg, 10 μmol), and $\text{P}(\text{fur})_3$ (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 $\rightarrow$ 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): 3375m (br.), 3192w (br.), 2945m, 2868m, 2235w, 1699s, 1596m, 1457m, 1384m, 1090m. ^1H -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, (8s, 4 Me_2C); 1.21–1.15 (*m*, 3 (Me_2CH)₃Si); 1.13–1.10 (*m*, 3 (Me_2CH)₃Si); 1.09–1.05 (*m*, (Me_2CH)₃Si); 1.04–1.01 (*m*, (Me_2CH)₃Si). ^{13}C -NMR (125 MHz, CDCl_3): see Table 8; additionally, 114.7, 114.0 (2 C), 113.3 (3s, 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)₃Si); 12.33, 12.28 (6 C), 12.0 (3*d*, 4 (Me_2CH)₃Si). HR-MALDI-MS (DHB): 1849.880 ($[M + \text{Na}]^+$, $\text{C}_{90}\text{H}_{138}\text{N}_8\text{NaO}_{24}\text{Si}_4^+$; 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), $[\text{Pd}_2(\text{dba})_3]$ (7.2 mg, 7.6 μmol), CuI (2.2 mg, 11 μmol), and P(fur)₃ (2.6 mg, 10 μmol) in degassed Et₃N/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), $[\text{Pd}_2(\text{dba})_3]$ (6.8 mg, 7.2 μmol), CuI (2.7 mg, 14 μmol), and P(fur)₃ (3.3 mg, 14 μmol) in degassed Et₃N/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*. ^1H -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)₃Si). HR-MALDI-MS (DHB): 2312.098 ($[M + \text{Na}]^+$, $\text{C}_{113}\text{H}_{172}\text{N}_{10}\text{NaO}_{30}\text{Si}_5^+$; 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), $[\text{Pd}_2(\text{dba})_3]$ (9.5 mg, 10 μmol), CuI (1.9 mg, 10 μmol), and P(fur)₃ (2.3 mg, 10 μmol) in degassed Et₃N/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. ^1H -NMR (300 MHz, CDCl_3): 7.24 (*d*, *J* = 8.0, H-C(6I)); 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)₃Si). MALDI-MS (indole-3-acetic acid): 2776.6 (100, $[M + \text{Na}]^+$).

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 (**16**). A soln. of **16** [4] (6.0 g, 10.9 mmol), **17** [4] (3.2 g, 10.4 mmol), $[\text{Pd}_2(\text{dba})_3]$ (494 mg, 0.52 mmol), CuI (198 mg, 1.0 mmol), and P(fur)₃ (241 mg, 1.0 mmol) in degassed Et₃N/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*. ^1H -NMR (400 MHz, CD_3OD): see Table 10; additionally, 7.78 (*d*, *J* = 8.1, H-C(6I)); 1.57, 1.53, 1.38, 1.34 (4s, 2 Me_2C); 0.98 (*t*, *J* = 7.5, (MeCH_2)₃Si); 0.58 (*q*, *J* = 7.5, (MeCH_2)₃Si). ^{13}C -NMR (100 MHz, CD_3OD): see Table 11; additionally, 115.3, 114.8 (2s, 2 Me_2C); 27.6, 27.5, 25.7, 25.4 (4*q*, 2 Me_2C); 7.8 (*q*, (MeCH_2)₃Si); 4.2 (*t*, (MeCH_2)₃Si). FAB-MS (NOBA): 729 (19, $[M + \text{H}]^+$), 713 (34, $[M - \text{Me}]^+$), 699 (21, $[M - \text{Et}]^+$). Anal. calc. for $\text{C}_{34}\text{H}_{44}\text{N}_4\text{O}_{12}\text{Si}$ (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)₂NH (3.5 ml, 25 mmol, distilled from CaH_2) in THF (100 ml) was treated dropwise with 1.65*M* 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*. ^1H -NMR (400 MHz, CD_3OD): see Table 10; additionally, 1.57, 1.55, 1.36, 1.35 (4s, 2 Me_2C); 0.98 (*t*, *J* = 7.5, (MeCH_2)₃Si); 0.59 (*q*, *J* = 7.5, (MeCH_2)₃Si). ^{13}C -NMR (100 MHz, CD_3OD): see Table 11; additionally, 115.0, 114.9 (2s, 2 Me_2C); 27.8, 27.5, 25.7, 25.5 (4*q*, 2 Me_2C); 7.8 (*q*, (MeCH_2)₃Si); 5.3 (*t*, (MeCH_2)₃Si). FAB-MS (NOBA): 855 (4, $[M + \text{H}]^+$).

Table 10. Selected ^1H -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
$J(1',2'/\text{I})$	2.4	1.9	2.4	1.4	1.5	2.0	1.5
$J(2',3'/\text{I})$	6.6	6.6	6.4	6.4	6.5	6.5	6.3
$J(3',4'/\text{I})$	4.3	3.6	3.0	3.7	4.2	4.1	4.4
$J(4',5'/\text{I})$	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)
$J(1',2'/\text{II})$	1.2	1.5	2.0	2.3	1.5	1.4	1.1
$J(2',3'/\text{II})$	6.5	6.6	6.5	6.5	6.5	6.5	6.4
$J(3',4'/\text{II})$	3.6	3.6	3.2	3.1	3.8	4.3	4.5
$J(4',5'/\text{II})$	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 CH₂Cl₂ (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 (Na₂SO₄), 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, CHCl₃). UV (MeOH): 276 (15000). IR (CHCl₃): 3385w, 2946m, 2868m, 2225w, 2175w, 1695s, 1595w, 1577w, 1384m, 1339w, 1265w, 1092m, 1068m. ¹H-NMR (400 MHz, CDCl₃): see Table 10, additionally, 9.55, 8.85 (2 br. s, 2 NH); 1.57, 1.55, 1.35, 1.33 (4s, 2 Me₂C); 1.23–1.15 (*m*, 2 (Me₂CH)₃Si); 1.13–1.08 (*m*, 2 (Me₂CH)₃Si); 0.94 (*t*, *J* = 7.5, (MeCH₂)₃Si); 0.55 (*q*, *J* = 7.5, (MeCH₂)₃Si). ¹³C-NMR (100 MHz, CDCl₃): see Table 11; additionally, 113.5, 113.4 (2s, 2 Me₂C); 27.2, 27.1, 25.2, 25.1 (4q, 2 Me₂C); 18.09, 18.06, 18.00 (6 C) (3q, 2 (Me₂CH)₃Si); 12.5, 12.3 (2d, 2 (Me₂CH)₃Si); 7.3 (*q*, (MeCH₂)₃Si); 4.2 (*t*, (MeCH₂)₃Si). MALDI-MS (indole-3-acetic acid): 1191 (100, [M + Na]⁺), 1207 (25, [M + K]⁺). Anal. calc. for C₅₂H₈₃IN₄O₁₂Si₃ (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-Pr)₂NH (3.4 ml, 24 mmol, distilled from CaH₂) 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. NaHCO₃ soln. and brine, dried (Na₂SO₄), 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, CHCl₃). UV (MeOH): 276 (16800). IR (CHCl₃): 3390w (br.), 3008w, 2944w, 2867w, 2220w, 1721s, 1697s, 1596w, 1433w, 1385m, 1341w, 1158m, 1087m, 1069m, 882m. ¹H-NMR (400 MHz, CDCl₃): see Table 10; additionally, 10.40, 9.70 (2 br. s, 2 NH); 1.60, 1.56, 1.37, 1.34 (4s, 2 Me₂C); 1.08–1.03 (*m*, (Me₂CH)₃Si). ¹³C-NMR (100 MHz, CDCl₃): see Table 11; additionally, 113.8, 113.3 (2s, 2 Me₂C); 27.3, 27.1, 25.5, 25.3 (4q, 2 Me₂C); 17.93, 17.90 (2q, (Me₂CH)₃Si); 11.9 (*d*, (Me₂CH)₃Si). FAB-MS (NOBA): 874 (80, [M + H]⁺), 858 (44, [M – Me]⁺), 829 (100, [M – Me₂C]⁺).

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 CH₂Cl₂ (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 (Na₂SO₄), 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, CHCl₃). UV (MeOH): 272 (15500). IR (CHCl₃): 3384w, 2945w, 2867w, 2220w, 1695s, 1595w, 1455m, 1384m, 1148w, 1089m, 1068m, 882w. ¹H-NMR (400 MHz, CDCl₃): see Table 10; additionally, 10.00, 9.50 (2 br. s, 2 NH); 1.57, 1.55, 1.35, 1.34 (4s, 2 Me₂C); 1.13–1.10 (*m*, (Me₂CH)₃Si); 1.07–1.02 (*m*, (Me₂CH)₃Si). ¹³C-NMR (100 MHz, CDCl₃): see Table 11; additionally, 113.6, 113.5 (2s, 2 Me₂C); 27.3, 27.2, 25.4, 25.3 (4q, 2 Me₂C); 17.95, 17.92 (2q, 2 (Me₂CH)₃Si); 12.3, 11.9 (2d, 2 (Me₂CH)₃Si). MALDI-MS (indole-3-acetic acid): 1051 (100, [M + Na]⁺), 1067 (20, [M + K]⁺). Anal. calc. for C₄₄H₆₉IN₄O₁₂Si₂ (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/H₂O/40% HF/37% HCl 100:50:2:2 (3 ml) was stirred at 40° for 100 h. Evaporation and HPLC (H₂O/MeOH 10:0 → 1:9) gave **24** (8 mg, 70%). White powder. $[\alpha]_D^{25} = +2.1$ (*c* = 0.53, H₂O). UV (MeOH): 276 (18300). IR (KBr): 3396s (br.), 2237w, 1686s, 1598m, 1460m, 1390s, 1267w, 1226w, 1109m, 1054m, 830w, 765w. ¹H-NMR (400 MHz, D₂O): see Table 12. ¹³C-NMR (100 MHz, D₂O): 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/H₂O/40% HF/37% HCl 100:50:2:2 (3 ml) was stirred at 40° for 125 h. Evaporation and HPLC (H₂O/MeOH 10:0 → 1:9) gave **25** (7.6 mg, 67%). White powder. $[\alpha]_D^{25} = +9.7$ (*c* = 0.35, H₂O). UV (MeOH): 283 (27400). IR (KBr): 3410s (br.), 2238w, 1686s, 1597m, 1458w, 1388m, 1113m, 1053m. ¹H-NMR (500 MHz, D₂O) see Table 12. ¹³C-NMR (125 MHz, D₂O): 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/H₂O/40% HF/37%

Table 12. Selected ^1H -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
$J(1',2'/\text{I})$	4.8	4.5	4.7
$J(1',2'/\text{II–V})$	4.1, 3.6	^c), 3.6, 4.5	6.0, 4.2, 4.2, 3.7
$J(2',3'/\text{I–V})$	5.5, 6.1, 6.4	5.7, ^c), ^c), 6.6	^c), ^c), ^c), ^c), 6.5
$J(3',4'/\text{I–V})$	4.0, 5.7, 3.2	3.6, 5.8, 5.8, 3.0	4.0, 5.9, 5.6, 5.9, 3.0
$J(4',5'/\text{I–II})$	4.2, 5.6	4.2, 5.8	6.2, 5.6
$J(4',5'/\text{III})$	3.3, 6.1	5.8	5.9
$J(4',5'/\text{IV})$	–	3.0, 5.9	6.8
$J(4',5'/\text{V})$	–	–	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 ($\text{H}_2\text{O}/\text{MeOH}$ 10:0 $\rightarrow$ 1:9) gave **26** (1.0 mg, 58%). White powder. UV (MeOH): 282 (37800). ^1H -NMR (500 MHz, D_2O): see Table 12. MALDI-MS (CCA): 1331.8 (100, $[M + \text{Na}]^+$), 1348.2 (20, $[M + \text{K}]^+$).

Synthesis of the rA_3 , 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 phosphoramidites 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-Pr) $_3\text{SiOCH}_2$ 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 $\text{NaH}_2\text{PO}_4/\text{Na}_2\text{HPO}_4$ buffer at pH 7 and at a 0.2M concentration of NaCl) in the cuvettes were overlaid with dimethylpolysiloxane.

REFERENCES

- [1] W. Czechtizky, X. Daura, A. Vasella, W. van Gunsteren, *Helv. Chim. Acta* **2001**, *84*, 2132.
- [2] W. Czechtizky, A. Vasella, *Helv. Chim. Acta* **2001**, *84*, 594.
- [3] W. Czechtizky, A. Vasella, *Helv. Chim. Acta* **2001**, *84*, 1000.
- [4] S. Eppacher, N. Solladié, B. Bernet, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1311.
- [5] H. Gunji, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 1331.
- [6] H. Gunji, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 2975.
- [7] H. Gunji, A. Vasella, *Helv. Chim. Acta* **2000**, *83*, 3229.
- [8] P. K. Bhardwaj, A. Vasella, *Helv. Chim. Acta* **2002**, *85*, 699.
- [9] A. J. Matthews, P. K. Bhardwaj, A. Vasella, *Chem. Commun.* **2003**, 950.

- [10] A. J. Matthews, P. K. Bhardwaj, A. Vasella, *Helv. Chim. Acta* **2004**, *87*, 2273.
- [11] H. C. Brown, B. Kanner, *J. Am. Chem. Soc.* **1953**, *75*, 3865.
- [12] X. Wu, S. Pitsch, *Nucleic Acids Res.* **1998**, *26*, 4315.
- [13] D. B. Davies, *Prog. Nucl. Magn. Reson. Spectrosc.* **1978**, *12*, 135.
- [14] T. D. W. Claridge, 'High-Resolution NMR Techniques in Organic Chemistry', Pergamon, Amsterdam, 1999, p. 142.
- [15] S. Pitsch, P. A. Weiss, X. Wu, D. Ackermann, T. Honegger, *Helv. Chim. Acta* **1999**, *82*, 1753.
- [16] U. Pieles, W. Zürcher, M. Schär, H. E. Moser, *Nucleic Acids Res.* **1993**, *21*, 3191.

Received August 27, 2004