Oligonucleotide Analogues with a 'Nucleobase-Including Backbone'

Part 10

Design, Synthesis, and Association of Ether-Linked Dimers

by **Andrew John Matthews**, **Punit Kumar Bhardwaj**, and **Andrea Vasella***

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

The dinucleoside analogues **24**, **25**, **28**–**30**, and **33** associate in $CDCl_3$ solution. Association constants, as determined from the concentration-dependent chemical shift for H–N(3) of the uridine moiety and from thermodynamic parameters, range from 265 M^{-1} (**33**) to 3220 M^{-1} (**30**). The association of **31** in $CDCl_3$ is too strong to be determined (concentration independent δ(H–N(3)) of *ca.* 12.8 ppm) and the fully deprotected dimer **32** proved insufficiently soluble in $CDCl_3$. This observation strongly evidences that structural differentiation of oligonucleotides and their analogues into backbone and nucleobases is not required for pairing. The dinucleotide analogues were prepared by *O*-alkylation of *C(8)*-unsubstituted or of *C(8)*-oxymethylated, partially protected adenosines by the *C(6)*-mesyloxy- or *C(6)*-halomethylated uridines **20**–**22**, followed by partial or total deprotection.

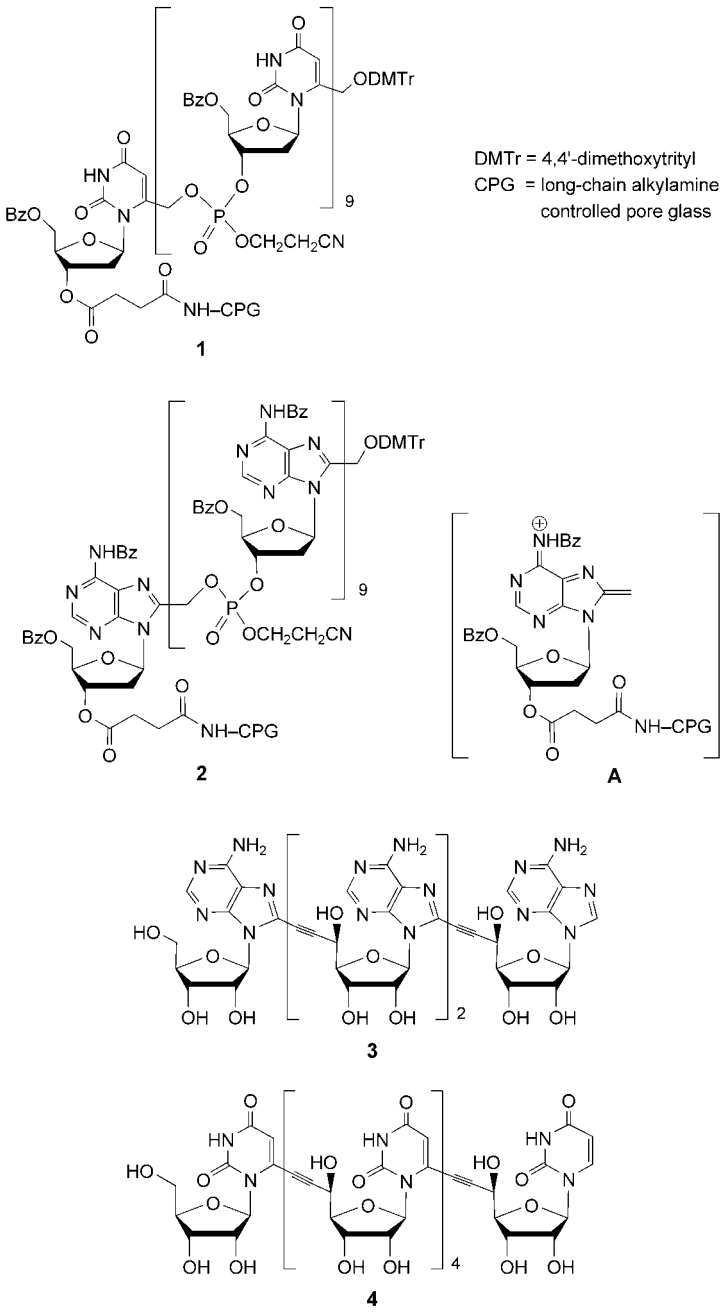
Introduction. – The most-conspicuous property of nucleic acids is their ability to form stable duplexes by selective base pairing, the sequence of bases leading to the structural diversity required for their biological role. In keeping with the central nature of this role, the structure of nucleic acids has been modified by changing the bases, the (deoxy)ribose moiety, and the phosphodiester linker, while maintaining the differentiation of nucleobase and backbone. This constant leads to the question of whether a dedifferentiation of backbone and nucleobase is compatible with pairing. We have attempted to answer this question by designing and synthesising oligonucleotide analogues that no longer differentiate between backbone and base [1].

We first prepared protected phosphodiester-linked decamers **1** and **2**, derived from *C(6)*-hydroxymethylated uridine dU*[1]) and *C(8)*-hydroxymethylated adenosine dA*, respectively [2–4]. Whilst decamer **1** was readily deprotected, the dA* decamer **2** decomposed, presumably by facile elimination of the phosphate group at $CH_2C(8)$, leading to the stabilised cation **A**.

A second-generation of neutral, ethynediyl-linked analogues is illustrated by the adenosine tetramer **3** [5–7] and uridine hexamer **4** [1][8] (*cf. Fig. 2*). The tetramer **3** proved poorly water-soluble, whilst the hexamer **4** showed the limits of the synthetic methodology. The pentamer corresponding to **4** did not undergo hetero-pairing with a

[1]) *Conventions for abbreviated notation:* The substitution at C(6) of pyrimidines and C(8) of purines is denoted by an asterisk (*); for example, dU* and dA* for the hydroxymethylated uridine and adenosine 2-deoxyribose derivatives, and U* and A* for the corresponding ribose derivatives. The moiety linking $C(6)CH_2$ or $C(8)CH_2$ and C(5′) of the previous unit is indicated in square brackets, such as -[O]- for oxygen.

complementary RNA heptamer. Modeling suggested that an *anti*-conformation of these analogues is a prerequisite for pairing, whilst NMR analysis of an adenosine dimer showed that a *syn*-conformation is preferred [9].



These results led us to design a third generation of analogues capable of duplex formation with bases in a *syn*-conformation. This is known to occur in Z-DNA [10][11], whose biological roles are drawing much interest [12]. A Me substituent at C(8) of guanine stabilises the *syn*-form of short oligonucleotides in a variety of sequences [13]. Modeling studies[2]) suggested that oxymethylene-bridged oligomers (*Fig. 1*) should form duplexes with a right-handed B-helix (seven residues per turn), maintaining a parallel orientation of *Watson–Crick* base pairs at a distance of 2.96 Å, comparable to the distance between base pairs in RNA duplexes (2.6–3.3 Å [10]).

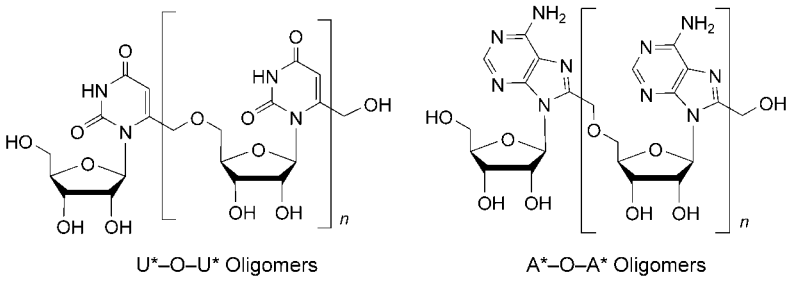


Fig. 1. *Oxymethylene-bridged analogues derived from U* and A**

Our initial goal was to prepare uridine U*-[O]-U*[1]), adenosine A*-[O]-A*, and self-complementary U*-[O]-A* and A*-[O]-U* dimers, and to analyse their pairing properties.

Results and Discussion. – 1. *Monomer Synthesis.* We have briefly communicated the preparation of the (4,4′-dimethoxytrityloxy)methyl adenosine **9** (*Scheme 1*) and the hydroxymethylated uridine **15** [15] (*cf. Scheme 2*), and we now provide details.

N^6-Benzoyl-2′,3′-*O*-isopropylideneadenosine (**5**) [16] was silylated to **6**, formylated [2][17], and then reduced to the *C(8)*-hydroxymethylated **7** (71% from **5**). This intermediate was, on the one hand, 4,4′-dimethoxytritylated to **8** and then desilylated to the alcohol **9** (84% from **7**). On the other hand, sequential deprotection of **7** by *N*-debenzoylation to **10** (96%), desilylation to **11** (87%), and deisopropylidenation yielded 8-(hydroxymethyl)adenosine (**12**; 92%).

The alcohols **5**, **9**, and **11** form a strong intramolecular H-bond from HO–C(5′) to N(3), as evidenced by δ(HO–C(5′)) in $CDCl_3$ (5.8–6.7 ppm), a small J(5′a,OH) ($\leq$2.2 Hz), a large J(5′b,OH) value ($\geq$10.3 Hz), and small J(4′,5′a) and J(4′,5′b) values ($\leq$ 2.2 Hz) indicating *anti*-periplanar H–C(4′) and C(5′)–O bonds (see [5]). This H-bond requires a *syn*-conformation, with the sugar adopting predominantly the (*S*)-conformation in $CDCl_3$ ((*S*)/(*N*) 77:23 to 83:17 as deduced from J(1′,2′)/J(3′,4′) in *Table 1*; [18]). A bifurcated intramolecular H-bond of HO(5′) to N(3) and O(4′) characterised by a O(5′)H···N(3) and O(5′)H···O(4′) distances of 1.92 and 2.48 Å is also found in the solid state of **11**[3]) (*Fig. 2*).

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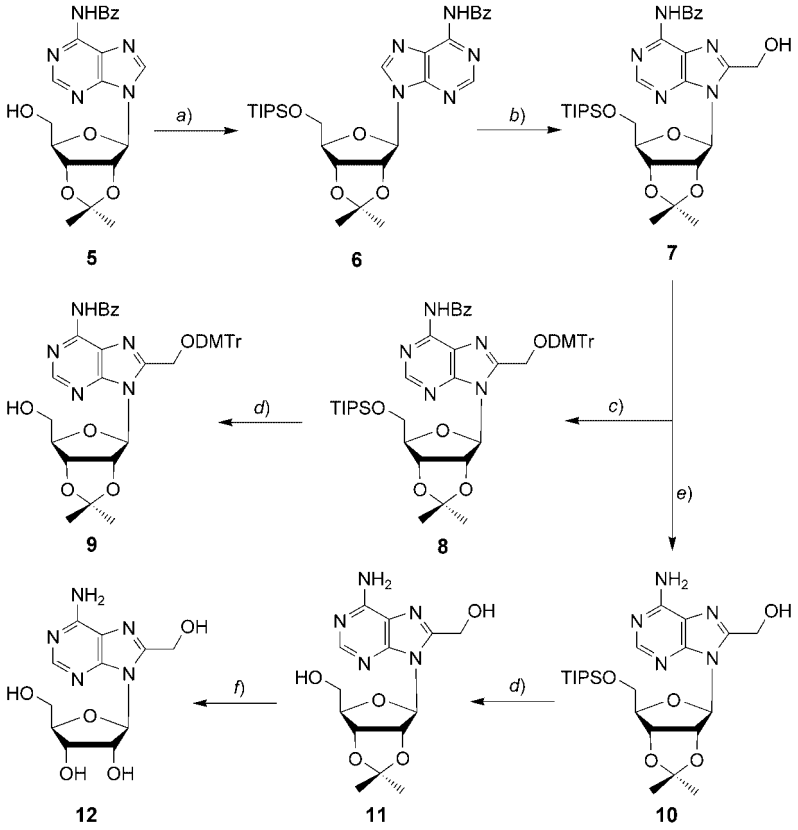
[2]) *Maruzen* model studies and *Macromodel* calculations using the Amber* force-field [14].

[3]) The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-216413 (**11**) and No. CCDC-216414 (**18**). Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

Scheme 1



DMTr = 4,4′-Dimethoxytrityl

a) (i-Pr)$_3$SiCl (TIPSCl), 1*H*-imidazole, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2; 96%. *b*) Lithium diisopropylamide (LDA), THF, then DMF, then AcOH, $-70°$, then EtOH, $NaBH_4$, 23°; 74%. *c*) DMTrCl, EtN(i-Pr)$_2$, DMAP, CH_2Cl_2; 94%. *d*) Bu_4NF (TBAF), THF; 89% of **9**; 87% of **11**. *e*) NH_3, H_2O/MeOH; 96%. *f*) HCO_2H/H_2O 4:1; 92%.

As a rule, the *syn*-conformation of 5′-*O*-protected adenosines is revealed by a downfield shift for H–C(2′) and an upfield shift for C(2′) [19]. The significant downfield shift for H–C(2′) ($\Delta\delta$(H–C(2′)) = 0.40–0.49 ppm), and upfield shift for C(2′) ($\Delta\delta$(C(2′)) = –1.4 to –1.8 ppm) of the *C(8)*-substituted silyl ethers **7**, **8**, and **10**, as compared to the corresponding signals for **6**, evidence that *C(8)*-substitution leads predominantly to a *syn*-conformation (*Table 1*). The *J*(4′,5′a) and *J*(4′,5′b) values for **7**, **8**, and **10** (5.6–6.5 Hz; see *Table 4* in *Exper. Part*) indicate some steric interaction between the nucleobase and the TIPSO–C(5′) (TIPS = (i-Pr)$_3$Si); the confomers possessing *anti*-periplanar H–C(4′) and H–C(5′) bonds are favoured. The (*S*)/(*N*) conformations of the fully protected derivatives **6** and **8** are equally populated in $CDCl_3$ (*J*(1′,2′)/*J*(3′,4′) = 47:53), whilst the methanols **7** and **10** slightly prefer the (*N*)-conformation (*J*(1′,2′)/*J*(3′,4′) = 39:61). The isopropylidenated silyl ethers **6**–**8** and **10**

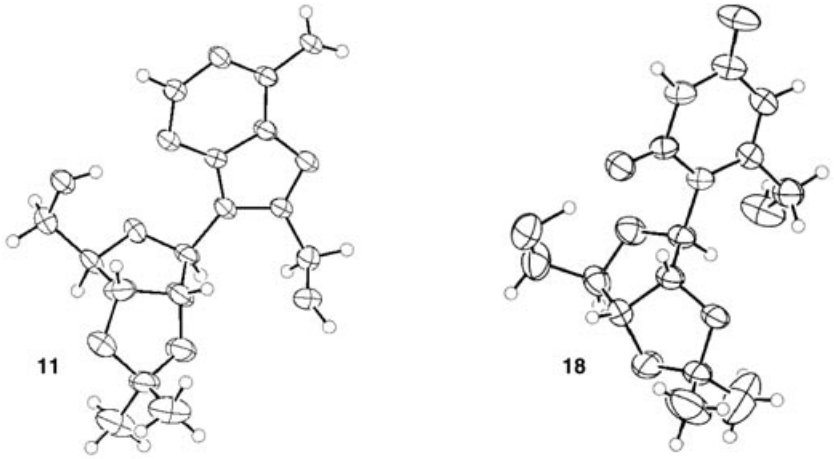


Fig. 2. *Crystal structures of the diols* **11** *and* **18**[3])

show a somewhat decreased ring pucker ($J(1',2')+J(3',4')=5.3-5.8$ Hz; see [20]), as compared to the isopropylidenated alcohols **5**, **9**, and **11** (6.0–6.5 Hz). De-isopropylidenation increases the ring pucker (9.1 Hz for **12**).

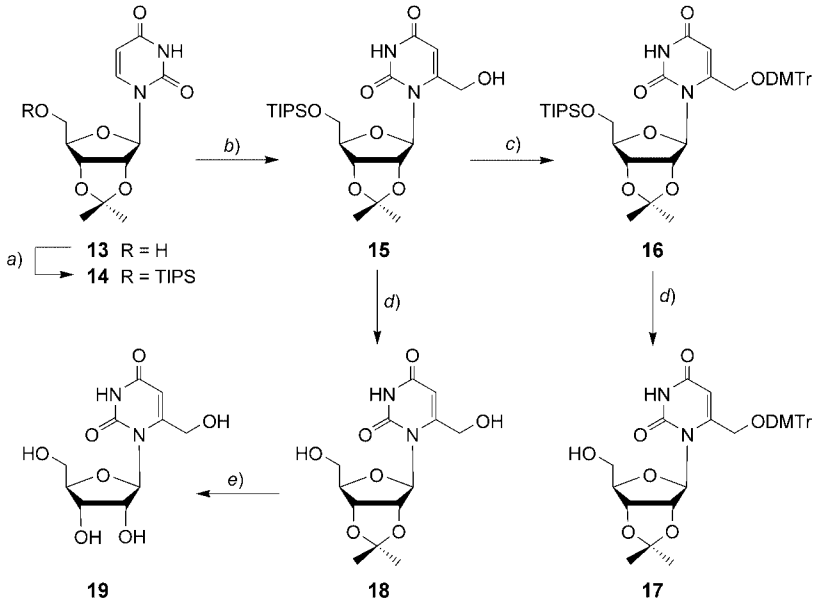
Table 1. *^{1}H- and ^{13}C-NMR Shift Differences for H–C(2′) and C(2′) of the Adenosine-Derived Monomers* **7**–**11** *as Compared to* **6**, *and the Uridine-Derived Monomers* **13** *and* **15**–**18** *as Compared to* **14**, *and Ratio of* (S)/(N)*-Conformers of these Nucleosides, as Deduced from* J(1′,2′)/J(3′,4′)

Nucleoside	Δδ(H–C(2′)) [ppm]	Δδ(C(2′)) [ppm]	$J(1',2')$ [Hz]	$J(3',4')$ [Hz]	(*S*)/(*N*)
5	−0.10	−1.5	5.0	1.2	81:19
6	[a])	[a])	2.5	2.8	47:53
7	0.40	−1.6	2.2	3.4	39:61
8	0.49	−1.8	2.7	3.1	47:53
9	−0.03	−2.0	5.0	1.5	77:23
10	0.41	−1.4	2.2	3.4	39:61
11	−0.04	−2.0	5.0	1.0	83:17
13	0.34	0.7	3.1	3.4	48:52
14	[b])	[b])	2.8	3.4	45:55
15	0.50	−1.3	1.2	4.5	21:79
16	0.50	−1.3	1.2	4.5	21:79
17	0.53	−2.2	2.5	3.9	39:61
18	0.55	−1.7	2.2	4.4	33:67

[a]) $\delta(H-C(2'))=5.32$ and $\delta(C(2'))=84.6$ ppm. [b]) $\delta(H-C(2'))=4.69$ and $\delta(C(2'))=85.4$ ppm.

The *C(6)*-hydroxymethylated **15** was prepared from the protected uridine **13** [21] by silylation to **14** [1], formylation [2][22], and reduction (67% from **13**; *Scheme 2*). The intermediate **15** was, on the one hand, 4,4′-dimethoxytritylated to **16** (95%), which was desilylated to the alcohol **17** (89%) and, on the other hand, desilylated to the diol **18** (89%) and further deisopropylidenated to 6-(hydroxymethyl)uridine (**19**; 90%).

Scheme 2



DMTr = 4,4′-Dimethoxytrityl

a) TIPSCl, 1*H*-imidazole, DMAP, CH_2Cl_2; 95%. *b*) LDA, THF, then DMF, then AcOH, −70°, then EtOH, $NaBH_4$, 23°; 70%. *c*) DMTrCl, $EtN(i\text{-}Pr)_2$, DMAP, CH_2Cl_2; 95%. *d*) TBAF, THF; 89% of **17**; 89% of **18**. *e*) HCO_2H/H_2O 4:1; 90%.

In polar solvents, like DMSO, uridines prefer the *anti*-conformation [23]. In apolar solvents, an intramolecular O(5′)H···O=C(2) H-bond may favour the *syn*-conformation [24]. The persistence of this H-bond may be derived from the *J*(5′a,OH) and *J*(5′b,OH) values [25]. MM3* Calculation and the *Karplus* equation of *Fraser et al.* [26] suggest *J*(5′a,OH) and *J*(5′b,OH) values of 0.5 and 11.5 Hz, respectively, for the intramolecularly H-bonded species of **13**. The $CDCl_3$ ^{1}H-NMR spectrum of a saturated solution of the sparingly soluble **13** shows broad signals of NH, HO−C(5′), and H_b−C(5′) due to solute−solute interactions. However, sharp signals for HO−C(5′), H_a−C(5′), and H_b−C(5′) of a one-third-saturated solution of **13** allowed us to assign *J*(5′a,OH) = 3.6 and *J*(5′b,OH) = 7.5 Hz (see *Table 6* in the *Exper. Part*), evidencing a partly persistent intramolecular H-bond. With 0.5 and 11.5 Hz as limiting values, 35% of **13** are engaged in an intramolecular H-bond. Substitution at C(6) enhances the persistence of the H-bond only slightly (42% for **17**; *J*(5′a,OH) = 3.1, *J*(5′b,OH) = 7.8 Hz), whilst broad signals for H−C(5′) and the OH groups prevented determination of the *J*(H,OH) values of **18**. In agreement with the enhanced persistence of the intramolecular H-bond, HO−C(5′) of **17** is shifted downfield (**13**: 2.62, **17**: 3.07 ppm). A bifurcated intramolecular H-bond of HO(5′) to O=C(2) and O(4′) is present in the solid state of **18** (*Fig. 2*; O(5′)H···O=C(2) = 1.71 and O(5′)H···O(4′) = 2.27 Å).

The chemical shift of H−C(2′) is a good indicator for the *syn*/*anti* equilibrium of uridines; 6-unsubstitued uridines prefer the *anti*-conformation [23]. H−C(2′) of

RO(5′)-protected derivatives of **13** (R = Me, Allyl, Pr, Bn, and Ac) resonates in $CDCl_3$ solution at 4.95–5.04 ppm [27][28]. Sterically demanding protecting groups at O(5′) disfavour the *syn*-conformer. Indeed, H–C(2′) of the TIPS-protected derivative **14** and its TBS analogue [29] resonate at the most-upfield position of O(5′)-protected derivatives of **13** (4.69–4.71 ppm). Presumably, these two silyl ethers prefer nearly exclusively the *anti*-conformation. Substitution at C(6) leads to a downfield shift for H–C(2′) of **15**–**18** ($\Delta\delta = 0.50$–0.55 ppm) and to an upfield shift for C(2′) ($\Delta\delta = 1.3$–2.2 ppm), evidencing a *syn*-conformation (*Table 1*). Apparently, the intramolecular H-bond of **17** and **18** has, at best, only a weak influence on the chemical shifts of H–C(2′) and C(2′). H–C(2′) of isopropylidenated uridines possessing sterically more-demanding alkyl substituents at C(6) resonates at 5.14–5.21 ppm ($\Delta\delta = 0.45$–0.52 ppm) [30], suggesting that such 6-alkylated uridines prefer exclusively the *syn*-conformation. H–C(2′) of **13** is shifted downfield by only 0.34 ppm indicating a *syn*/*anti* ratio of 65:35. Thus, the *syn*-conformation of **13** and **17** is distinctly more highly populated than suggested by the persistence of the intramolecular H-bond (65 and 100 *vs.* 35 and 42%, resp.). The partly persistent intramolecular C(5′)–OH···O=C(2) H-bond of **13**, **17**, and **18** is also evidenced by small $J(4',5'a)$ and $J(4',5'b)$ values (2.3–5.3 Hz; see *Table 6* in the *Exper. Part*). Larger $J(4',5'a)$ and $J(4',5'b)$ values of the silyl ethers **15** and **16** (5.7–6.9 Hz) evidence a steric interaction between the nucleobase and TIPSO–C(5′); the conformer with *anti*-periplanar H–C(4′) and H–C(5′) bonds is favoured. Solutions of the *C(6)*-unsubstituted **13** and **14** in $CDCl_3$ are characterised by a *ca.* 1:1 (*S*)/(*N*) equilibrium ($J(1',2')/J(3',4') = 48:52$ and 45:55, resp., *cf. Table 1*), whilst the *C(6)*-substituted silyl ethers **15** and **16** adopt predominantly the (*N*)-conformation ($J(1',2')/J(3',4') = 21:79$). The 6-substituted alcohols **17**, **18**, and **19** have a smaller preference for the (*N*)-conformer ($J(1',2')/J(3',4') = 39:61$, 33:67, and 40:60, resp.). The isopropylidenated compounds show a similar ring puckering ($J(1',2') + J(3',4') = 5.7$–$6.6$ Hz), which is increased by deisopropylidenation (10.3 Hz for **19**).

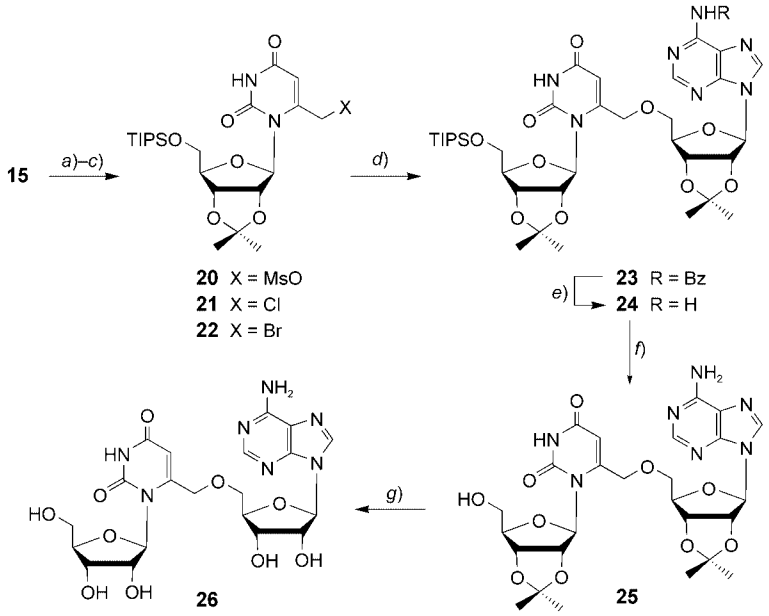
2. *Dimer Synthesis.* We first prepared the self-complementary U*-[O]-A and U*-[O]-A* dimers **23**–**32** (*Schemes 3* and *4*). The synthesis of **27**–**32** was briefly communicated [15]. The electrophiles **20**–**22** required for the ether formation were prepared from the alcohol **15** by mesylation (Ms_2O) to form the unstable mesylate **20** (90%), chlorination to **21** (*via* **20**, using MsCl, 95%), and bromination with PBr_3 to **22** (67%). *O*-Alkylation of the *C(8)*-unsubstituted adenosine derivative **5** (*Scheme 1*) gave the U*-[O]-A dimer **23** (45% from **20**; 62% from **21**; 60% from **22**). *N*-Debenzoylation of **23** gave the amine **24** (98%), which was desilylated to the alcohol **25** (80%), and further deprotected [7] to yield 93% of the fully deprotected **26**.

The *C(8)*-substituted adenosine derivative **9** (*Scheme 1*) was *O*-alkylated by **21** to the U*-[O]-A* dimer **27** (63%; *Scheme 4*). *N*-Debenzoylation of **27** gave the amine **28** (98%). Detritylation or desilylation of **28** led to the monoalcohols **29** (85%) and **30** (71%), respectively, which were further deprotected to the same diol **31** (86 and 81%, resp.). Hydrolysis yielded the completely deprotected dimer **32** (89%).

The ^{1}H-NMR spectra of the debenzoylated dimers **24**, **25**, and **28**–**31** in $CDCl_3$ are characterised by a concentration-dependent downfield shift of the uridine H–N(3), evidencing an intermolecular H-bond.

The *syn*-conformation of the adenosine unit (unit I) of the U*-[O]-A dimers **23**–**25** in $CDCl_3$ is more highly populated than the *syn*-conformation of **6**, as evidenced by

Scheme 3



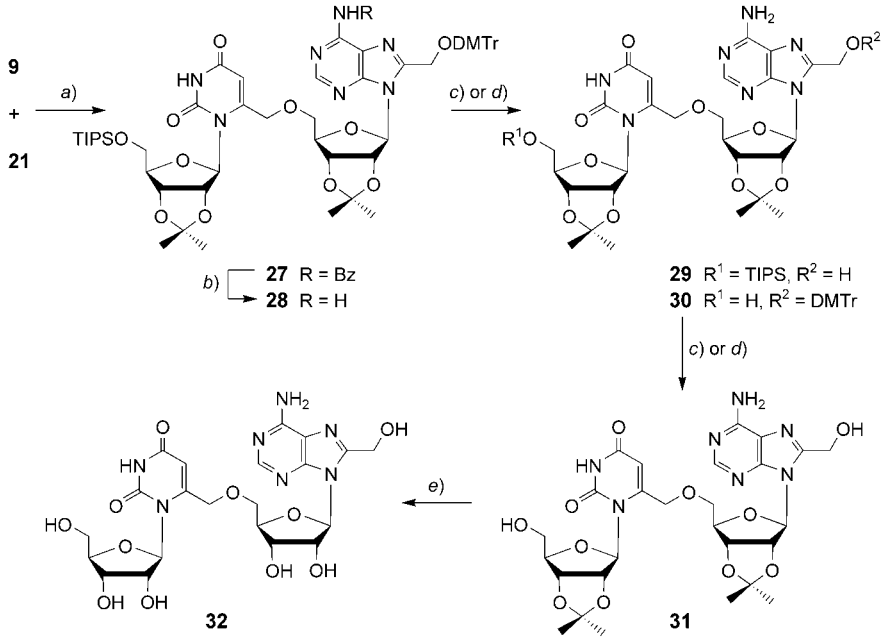
a) Ms_2O, Et_3N, CH_2Cl_2; 90% of **20**. *b*) MsCl, DMAP, pyridine; 95% of **21**. *c*) CaH_2, Br_3P, Et_2O; 67% of **22**. *d*) NaH, **5**, DMF/THF 2:1; 45% from **20**; 62% from **21**; 60% from **22**. *e*) NH_3, H_2O/MeOH; 98%. *f*) TBAF, THF; 80%. *g*) HCO_2H/H_2O 4:1; 93%.

$\Delta\delta(H-C(2'))=0.34-0.43$ ppm and $\Delta\delta(C(2'))=-0.4$ ppm (*Table 2*). This probably reflects the weaker steric hindrance by the uridinemethoxy moiety than by the TIPSO group. As expected, the U*-[O]-A* dimers **27**–**30** show an even stronger preference for a *syn*-conformation ($\Delta\delta(H-C(2'))=0.38-0.71$ ppm, $\Delta\delta(C(2'))=-1.0$ to -1.2 ppm). The steric repulsion between the nucleobase and the uridinemethoxy moiety is stronger in **27**–**31** than in **23**–**25**, as evidenced by larger $J(4',5'a)$ and $J(4',5'b)$ values (3.4–5.7 *vs.* 2.7–3.3 Hz; see *Table 8* in the *Exper. Part*). Unit I prefers a (*N*)-conformation, and debenzoylation increases this preference ($J(1',2')/J(3',4')=43:57$ and 33:67 for **23** and **27**, resp., as compared to 23:77 to 32:68 for **24**, **25**, and **28**–**30**). In the isopropylidenated dimers, the ring pucker in unit I dimers is larger for U*-[O]-A* ($J(1',2')+J(3',4')\approx 5-6.4$ Hz) than for U*-[O]-A (*ca.* 5–5.7 Hz)[4]). Deisopropylidenation increases the ring pucker (9.0 and 10.1 Hz for **26** and **32**, resp.).

The uridine unit (unit II) of the U*-[O]-A dimers **23**–**25** and of the U*-[O]-A* dimers **27**–**30** prefers a *syn*-conformation ($\Delta\delta(H-C(2'))=0.46-0.70$ ppm, $\Delta\delta(C(2'))=-1.0$ to -1.3 ppm relative to **14**; *Table 2*). The $J(4',5'a)$ and $J(4',5'b)$ values for the silyl ethers **23**, **24**, and **27**–**29** (5.3–7.1 Hz; see *Table 8* in the *Exper. Part*)

[4]) There appears to be a correlation between the population of the *syn*-conformation and ring pucker in unit I, with an increase in the *syn*-population leading to an increase of ring pucker. This correlation can also be seen for the adenosine silyl ethers **7**, **8**, and **10** as compared to **6**. No correlation is seen for the uridine monomers **15** and **16**, as compared to **14**.

Scheme 4



DMTr = 4,4′-Dimethoxytrityl

a) NaH, DMF/THF 2:1; 63%. *b*) NH_3, H_2O/MeOH; 97%. *c*) HCO_2H, $MeNO_2$; 85% of **29**; 86% of **31**. *d*) TBAF, THF; 71% of **30**; 81% of **31**. *e*) HCO_2H/H_2O 4:1; 89%.

Table 2. *^{1}H- and ^{13}C-NMR Shift Differences for H−C(2′) and C(2′) of the U*-O-A Dimers* **23**–**25**, *and the U*-O-A* Dimers* **27**–**30** *in $CDCl_3$, as Compared to the Adenosine-Derived Monomer* **6** *and the Uridine-Derived Monomer* **14**, *and the Ratio of* (S)/(N)*-Conformers of these Nucleosides, as Deduced from* J(1′,2′)/J(3′,4′)

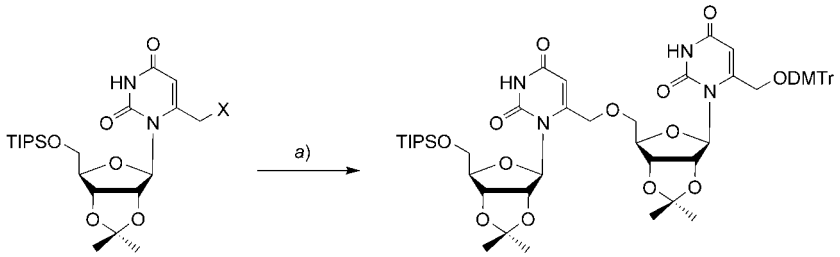
Nucleoside	**6**	**14**	**23**	**24**	**25**	**27**	**28**	**29**	**30**
Adenosyl unit I									
Δδ(H−C(2′)) [ppm]	[a])	–	0.43	0.34	0.36	0.38	0.56	0.71	0.43
Δδ(C(2′)) [ppm]	[a])	–	−0.4	−0.4	1.2[b])	−1.2	−1.0	−1.2	−1.0
J(1′,2′) [Hz]	2.5	–	1.6	1.1	1.0	2.1	1.3	<1.0	1.2
J(3′,4′) [Hz]	2.8	–	2.1	2.3	2.2	4.2	3.8	3.3	3.7
(*S*)/(*N*)	47:53	–	43:57	32:68	31:69	33:67	25:75	23:77	24:76
Uridyl unit II									
Δδ(H−C(2′)) [ppm]	–	[c])	0.47	0.59	0.57	0.52	0.58	0.71	0.60
Δδ(C(2′)) [ppm]	–	[c])	−1.2	−1.0	0.4[b])	−1.3	−1.0	−1.1	−1.3
J(1′2′) [Hz]	–	2.8	1.0	<1.0	1.2	<1.0	<1.0	<1.0	1.9
J(3′,4′) [Hz]	–	3.4	4.3	4.4	4.5	4.5	4.5	4.7	4.5
(*S*)/(*N*)	–	45:55	19:81	19:81	21:79	18:82	18:82	18:82	30:70

[a]) δ(H−C(2′)) = 5.32 and δ(C(2′)) = 84.6 ppm. [b]) From a CD_3OD spectrum. [c]) δ(H−C(2′)) = 4.69 and δ(C(2′)) = 85.4 ppm.

reflect a steric interaction between the nucleobase and TIPSO–C(5′), whilst lower values for the alcohols **25** and **30** (2.4–4.2 Hz) are in keeping with a partly persistent intramolecular O(5′)H ··· O=C(2) H-bond. Unfortunately, HO–C(5′/II) of **25** and **30** could not be assigned in the $CDCl_3$ ^{1}H-NMR spectra. Unit II of **23**–**25** and **27**–**29** shows a larger preference for a (*N*)-conformation than unit I (*cf. Table 2*). This is not so for the alcohol **30** (30:70), on account of the intramolecular H-bond. The isopropylidenated U*-[O]-A and U*-[O]-A* dimers show similar ring puckering in unit II ($J(1',2')+J(3',4')\approx 5.0-5.7$ Hz), with the exception again of **30** (6.4 Hz). Deisopropylidenation increases the ring pucker (9.0 and 9.9 Hz for **26** and **32**, resp.).

We abstained from preparing U*-[O]-U dimers, as base treatment of 2′,3′-*O*-isopropylideneuridine (**13**) leads to an intramolecular β-addition [31]. The *C(6)*-substituted alcohol **17** (*Scheme 2*), however, prefers a *syn*-conformation preventing such a β-addition, and *O*-alkylation of **17** with the mesylate **20**, chloride **21**, or bromide **22** gave the protected U*-[O]-U* dimer **33** (29% from **20**; 35% from **21**; 50% from **22**; *Scheme 5*).

Scheme 5



20 X = MsO
21 X = Cl
22 X = Br

33

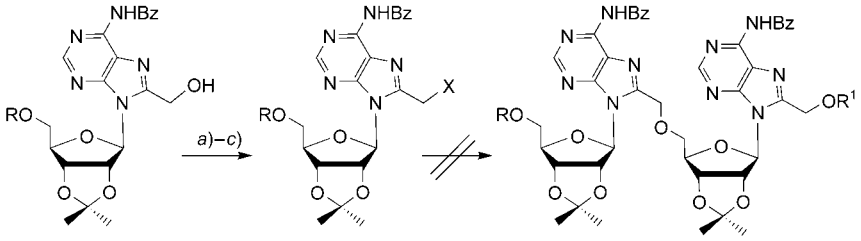
DMTr = 4,4′-Dimethoxytrityl

a) NaH, **17**, DMF/THF 2:1; 29% from **20**; 35% from **21**; 50% from **22**.

The ^{1}H-NMR spectra of the U*-[O]-U* dimer **33** in $CDCl_3$ is characterised by a concentration-dependent downfield shift of H–N(3) of units I and II, evidencing intermolecular H-bonds. The *syn*-conformation of both units in $CDCl_3$ is more highly populated than the *syn*-conformation of **14**, as evidenced by $\Delta\delta(H-C(2'))=0.49-0.52$ ppm and $\Delta\delta(C(2'))=-1.0$ to -1.2 ppm. The large $J(4',5')$ values of 6.5–7.5 Hz reflect a steric interaction between the nucleobase and the substituent at O(5′); the conformers possessing antiperiplanar H–C(4′) and H–C(5′) bonds are favoured. Units I and II both prefer the (*N*)-conformation ($J(1',2')/J(3',4')=18:82$ and 19:81, resp.).

The hypothesis that the strand breaks observed upon the attempted deprotection of the dA* decamer **2** are due to facile elimination of the phosphate group at CH_2–C(8), and generation of the stabilised cation **A** [2] suggested to prepare the A*-[O]-A* dimer by addition–elimination. The trichloroacetimidate **36** (86%) was thus prepared from

Scheme 6



34 R = Et_3Si
35 R = Me_2(thexyl)Si
36 R = Et_3Si, X = $Cl_3CC(NH)O$
37 R = Me_2(thexyl)Si, X = MsO
38 R = Me_2(thexyl)Si, X = Cl

Thexyl = 1,1,2-trimethylpropyl
a) **34**, Cl_3CCN, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), CH_2Cl_2; 86% of **36**. *b*) **35**, Ms_2O, Et_3N, CH_2Cl_2; 85% of **37**. *c*) **35**, MsCl, Et_3N, LiCl, CH_2Cl_2; 74% of **38**.

the alcohol **34**, and the unstable mesylate **37** (50–90%) and the chloride **38** (74%) were obtained from the alcohol **35** (*Scheme 6*)[5]).

The trichloroacetimidate **36** did, however, not react with the alcohols **5** or **9** (*Scheme 1*) in the presence of catalytic amounts of MsOH, CSA (=camphorsulfonic acid), $BF_3 \cdot OEt_2$, or TMSOTf in CH_2Cl_2, cyclohexane, Et_2O, THF, MeCN, or *N*,*N*-dimethylpivalamide. With a molar equivalent of these acids, or a stronger acid such as TfOH or HBF_4, increasing the temperature, or prolonging the reaction time led to deprotection and side reactions. Addition of NaH or lithium tetramethylpiperidide to deprotonate the *N(6)*-benzamido group and force the elimination led to decomposition of the trichloroacetimidate **36**. Similarly, base-promoted *O*-alkylation of the alcohols **5** or **9** with the mesylate **37** or the chloride **38** led to decomposition of the electrophile; the alcohol was recovered. Some N^6-alkylation products were observed, as evidenced by ^{1}H-NMR and MS.

3. *Association of the Dimers.* Association constants K_a and the thermodynamic parameters ΔH°, ΔS° and ΔG° in $CDCl_3$ were calculated for the U*-[O]-A dimers **24** and **25**, and for the U*-[O]-A* dimers **28**–**30** from the concentration and temperature dependence of δ(H–N(3)) (*Fig. 3* and *Table 3*). The association constant K_a in $CDCl_3$ was also calculated for the U*-[O]-U* dimer **33**. The $\Delta\delta$(H–N(3)) value of the diol **31** in $CDCl_3$ was almost concentration-independent (12.96–12.65 ppm for 33–1 mM), evidencing a strong association. The fully deprotected dimers **26** and **32** were not sufficiently soluble in $CDCl_3$ to determine their association. The δ(H–N(3)) value of the dimers is about the same as for the monomers in (D_5)pyridine and (D_6)DMSO.

These results support the contention that the structural differentiation between nucleobases and backbone is not required for association.

The K_a values compare favourably with that determined for the interaction of 3′,5′-di-*O*-acetyl-2′-deoxyuridine with 3′,5′-di-*O*-acetyl-2′-deoxyadenosine (70 M^{-1} [32]) and for the interaction of 9-ethyladenine and 1-cyclohexyluracil (110 ± 9 M^{-1} [33]). The

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[5]) We thank *Anne Viger* for the experiments with the thexyldimethylsilyl ether **35** (*A.V.* Ph.D. thesis, in preparation).

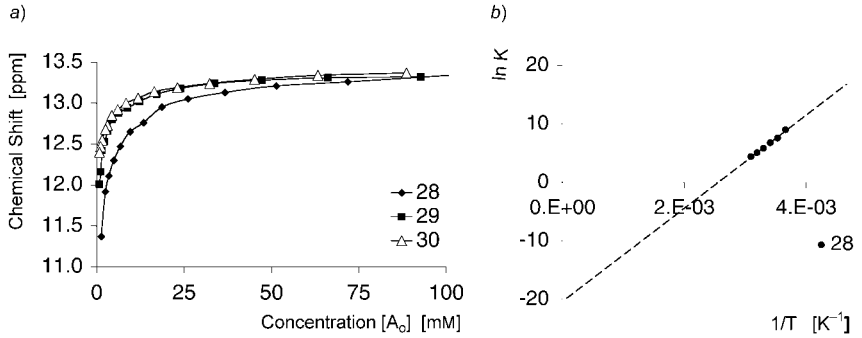

Fig. 3. *a) Dependence of δ(H–N(3)) of the U*-O-A* dimers* **28**–**30** *upon the concentration.* b) Van't Hoff *correlation for the U*-O-A* dimer* **28**.

Table 3. *Association Constants and Thermodynamic Parameters for the U*-O-A Dimers* **24** *and* **25**, *the U*-O-A* Dimers* **28**–**30**, *and Association Constant and ΔG for the U*-O-U* Dimer* **33**

Dimer	K_a [M^{-1}]	$-\Delta H$ [kcal/mol]	$-\Delta S$ [e.u.]	$-\Delta G$ [kcal/mol][a])	
24	1890	22	62	4.0	4.4
25	2500	13	30	4.6	4.2
28	970	16	40	4.0	3.9
29	280	22	64	3.3	3.0
30	3220	24	65	4.7	5.3
33	265	–	–	3.3	

[a]) The first value is calculated from K_a, the second from ΔH and ΔS.

high K_a values for **25** and **30**, and the inability to dissociate **31** appreciably in $CDCl_3$ correlate with a downfield shift of HO–C(5′) as compared to **13** ($\Delta\delta$ *ca.* 1.0 ppm). This downfield shift evidences an intramolecular C(5′)O–H···O=C(2) H-bond that may, in its turn, be correlated with the observation that the dimers **25**, **30**, and **31** possessing a HO–C(5′/II) group have higher association constants than the corresponding silyl ethers **24**, **28**, and **29**. This higher association constant is, thus, interpreted as the result of a more-favourable pairing conformation ('preorganisation') rather than a reduced steric hindrance of the alcohols. The data for the silyl ethers **28** and **29** highlight the contribution of the lipophilic DMTr group. Substitution at C(8) of the adenine unit increases the K_a value for the HO–C(5′/II) dimer **30**, but decreases the K_a value for the silyl ether **29**.

Cross-peaks between the H-bonded imino H–N(3) and adenine H–C(2) and H–C(8) in a 2D-NOESY experiment on the associated dimer **24** suggest both *Watson–Crick*- and *Hoogsteen*-type base pairing [32][33]. A cross-peak between the H-bonded imino H–N(3) and adenine H–C(2) in a 2D-NOESY experiment on the associated dimer **28** suggests *Watson–Crick*-type base pairing, but this experiment can not detect *Hoogsteen*-type base pairing, as there is no H–C(8). It has been suggested that a H–C(2) downfield shift implies *Watson–Crick* H-bonds, and that a H–C(8) downfield shift implies interactions of the *Hoogsteen*-type [34][35]. There is a small upfield shift for H–C(8) of the adenine unit of the associated dimer **24** ($\Delta\delta =$

0.11 ppm) and for the associated dimer **25** ($\Delta\delta = 0.14$ ppm) as compared to the monomer 2′,3′-*O*-isopropylidene-5′-*O*-(triethylsilyl)adenosine ($\delta = 8.07$ ppm [6]). The chemical shift for H–C(2) does not change ($\delta = 8.37 - 8.38$ ppm).

Although the thermodynamic parameters for the association listed in *Table 3* suggest that there are two groups of dimers (**24**, **29**, and **30** *vs.* **25** and **28**) and evidence enthalpy/entropy compensation [36], there is no obvious correlation with structural parameters; such a correlation requires the synthesis and study of the association of further 'structurally dedifferentiated' di- and oligonucleosides.

We thank the *ETH-Zürich* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

General. THF was distilled from Na/benzophenone. CH_2Cl_2, DMF, pyridine, diisopropylamine ($^iPr_2NH$), and ethyl(diisopropyl)amine (EtN^iPr_2) were distilled from CaH_2. Reactions were run under Ar or N_2. 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. Workup: org. phases were dried (Na_2SO_4), filtered, and processed as indicated. 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% in the indicated solvent or solid state (ATR). ^{1}H- and ^{13}C-NMR: at 300, 400, or 500 MHz and at 75, 100, or 125 MHz, resp. MS: matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS), indol-3-acrylic acid (IAA), 0.05M in THF or α-cyano-4-hydroxycinnamic acid (CCA) 0.05M in MeCN/EtOH/H_2O, and 2,5-dihydroxybenzoic acid (DHB) 0.05M in THF for high-resolution (HR) MALDI-MS.

General Procedure for NMR Studies. NMR Spectra were recorded at 295 K on a *Varian Gemini 300* spectrometer (300 MHz) in $CDCl_3$ passed through basic aluminum oxide immediately prior to use. Experiments started at the highest indicated concentration, with stepwise replacement of 0.2 ml of the 0.7 ml soln. with 0.2 ml of pure $CDCl_3$. The data were analysed graphically [37] and by nonlinear least-squares fitting [38]. Thermodynamic parameters were determined by *van't Hoff* analysis. The uridyl δ(H–N(3)) was monitored between 50° and −30° at a fixed concentration (between 20–80% of saturation).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-5′*-O-*(triisopropylsilyl)adenosine* (**6**). A soln. of **5** [16] (10.0 g, 24.3 mmol), 1*H*-imidazole (3.34 g, 48.6 mmol), and DMAP (0.30 g, 2.4 mmol) in CH_2Cl_2 (155 ml) was treated dropwise at 23° with TIPSCl (10.84 ml, 48.6 mmol), stirred for 3 h, washed with H_2O (2 × 70 ml) and brine (1 × 70 ml), dried ($MgSO_4$), and adsorbed onto silica (25 g). FC (silica gel (500 g); AcOEt/cyclohexane 1:1) gave **6** (13.24 g, 96%). White solid. R_f (AcOEt) 0.56. M.p. 60–62°. $[\alpha]_D^{25} = -34.6$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3411*w*, 3012*m*, 2961*m*, 2947*m*, 2895*w*, 2869*m*, 1710*m*, 1613*s*, 1586*m*, 1505*w*, 1456*m*, 1385*m*, 1261*s*, 1092*s*, 1014*m*, 881*m*, 808*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 9.34 (br. *s*, NH); 8.81 (*s*, H–C(2)); 8.21 (*s*, H–C(8)); 8.04–8.00 (*m*, 2 arom. H); 7.61–7.46 (*m*, 3 arom. H); 1.64, 1.41 (2*s*, Me_2C); 1.03–0.98 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 164.53 (*s*, C=O); 133.63 (*s*); 132.55 (*d*); 128.65 (2*d*); 127.81 (2*d*); 114.27 (*s*, Me_2C); 27.28, 25.44 (2*q*, Me_2C); 17.98 (*q*, $(Me_2CH)_3Si$); 11.93 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 568.2955 (100, $[M+H]^+$, $C_{29}H_{42}N_5O_5Si^+$; calc. 568.2956), 590.2766 (80, $[M+Na]^+$, $C_{29}H_{41}N_5NaO_5Si^+$; calc. 590.2777).

N^6-*Benzoyl-8-(hydroxymethyl)-2′,3′*-O-*isopropylidene-5′*-O-*(triisopropylsilyl)adenosine* (**7**). A soln. of $^iPr_2NH$ (14.2 ml, 100.3 mmol) in THF (57 ml) was cooled to −78°, treated dropwise with 1.6M BuLi in hexane (62.7 ml, 100.3 mmol), stirred for 15 min, warmed to 0°, stirred for 15 min, cooled to −78°, and treated dropwise with a soln. of **6** (10.65 g, 20.07 mmol) in THF (81 ml) over 10 min, stirred for 1 h, treated with DMF (38.8 ml, 501.4 mmol), stirred for 2.5 h, treated with AcOH (14.3 ml), allowed to warm to 23°, diluted with EtOH (142 ml), treated slowly with $NaBH_4$ (2.34 g, 60.2 mmol), and stirred for 25 min. After evaporation, the residue was dissolved in CH_2Cl_2 (200 ml), washed with H_2O (2 × 100 ml) and brine (1 × 100 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (500 g); AcOEt/cyclohexane 1:1 → AcOEt) gave **7** (8.88 g, 74%). White solid. R_f (AcOEt) 0.46. M.p. 93–95°. $[\alpha]_D^{25} = -10.8$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3610*w*, 3410*w* (br.), 3013*m*, 2961*m*, 2947*m*, 2894*m*, 1709*m*, 1615*s*, 1591*m*, 1479*s*, 1462*s*, 1430*m*, 1258*s*, 1092*s*, 1075*s*, 883*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 9.50 (br. *s*, NH); 8.01–7.97 (*m*, 2 arom. H); 7.53–7.39 (*m*, 3 arom. H); 5.85 (br. *s*, OH); 1.59, 1.42 (2*s*, Me_2C); 1.00–0.90 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see

Table 4. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Adenosine Monomers* **5**–**11** *and* **36**–**38** *in $CDCl_3$, and of* **12** *in CD_3OD*

	5 [5]	**6**[a])	**7**[a])	**8**[a])	**9**	**10**	**11**[a])	**12**	**36**	**37**	**38**
H–C(1′)	5.95	6.22	6.29	6.27	6.16	6.25	6.10	6.13	6.38	6.22	6.32
H–C(2′)	5.22	5.32	5.72	5.81	5.29	5.73	5.28	4.93	5.88	5.77	5.83
H–C(3′)	5.10	5.05	5.12	5.11	5.12	5.13	5.04	4.35	5.13	5.06	5.13
H–C(4′)	4.54	4.43	4.25	4.23	4.48	4.27	4.49	4.19	4.26	4.29	4.30
H_a–C(5′)	3.98	3.96	3.77	3.91	4.01	3.83	3.93	3.89	3.79	3.76	3.75
H_b–C(5′)	3.80	3.84	3.65	3.74	3.84	3.70	3.77	3.73	3.67	3.64	3.62
H–C(2)	8.76	8.81	8.65	8.77	8.77	8.24	8.10	8.12	8.85	8.79	8.81
H–C(8)	8.08	8.21	–	–	–	–	–	–	–	–	–
CH_a–C(8)	–	–	4.96	4.54	4.51	4.94	4.85	4.90	5.71	5.57	4.92
CH_b–C(8)	–	–	4.90	4.49	4.45	4.88	4.80	4.80	5.64	5.57	4.92
J(1′,2′)	5.0	2.5	2.2	2.7	5.0	2.2	5.0	7.5	2.1	2.7	2.4
J(2′,3′)	5.9	6.2	6.5	6.5	5.9	6.5	5.6	5.3	6.5	6.3	6.3
J(3′,4′)	1.2	2.8	3.4	3.1	1.5	3.4	1.0	1.6	3.3	3.3	3.5
J(4′,5′a)	1.9	4.4	6.2	6.5	1.2	5.9	< 1.0	2.2	5.4	5.7	6.0
J(4′,5′b)	2.2	4.4	5.6	6.2	2.1	5.9	< 1.0	2.2	5.8	6.0	5.7
J(5′a,5′b)	12.5	11.1	10.4	10.3	12.8	10.8	12.0	12.8	10.8	10.8	11.9
J(5′a,OH)	2.2	–	–	–	1.8	–	< 2.0	–	–	–	–
J(5′b,OH)	10.9	–	–	–	10.9	–	10.3	–	–	–	–
J(H_a,H_b)	–	–	15.9	12.1	12.1	15.5	16.0	14.5	13.1	[b])	15.3

[a]) Assignment based on selective homodecoupling experiments. [b]) Not determined.

Table 5. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Adenosine Monomers* **5**–**11** *and* **36**–**38** *in $CDCl_3$, and* **12** *in (D_6)DMSO*

	5 [5]	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**36**	**37**	**38**
C(1′)	94.11	91.38	89.85	90.52	92.34	89.84	91.74	88.76	90.20	90.41	90.42
C(2′)	83.07	84.60	83.00	82.83	82.58	83.25	82.65	72.42	83.18	82.81	83.24
C(3′)	81.55	81.26	81.45	82.14	81.27	81.42	81.53	71.06	81.44	81.43	81.59
C(4′)	86.20	87.40	87.50	87.43	85.58	87.48	85.70	86.60	87.60	87.27	87.65
C(5′)	63.26	63.49	62.94	63.42	63.31	63.02	63.05	62.32	63.03	62.63	62.83
C(2)	152.19	152.70	152.12	152.25	151.99	152.78	152.14	151.96	153.02	153.29	152.58
C(4)	150.11	149.51	148.71	149.02	149.73	150.37	149.29	149.73	149.72	149.97	150.51
C(5)	124.20	123.10	121.03	121.78	122.41	117.84	118.18	118.12	121.66	122.08	122.26
C(6)	150.20	151.02	151.90	151.93	151.37[a])	154.90	155.13	156.18	152.14	152.24	152.58
C(8)	142.39	141.45	154.39	151.93	151.43[a])	151.84	150.93	151.13	148.74	147.19	149.77
CH_2–C(8)	–	–	57.48	59.48	59.52	57.26	57.14	56.58	62.55	62.33	36.73

[a]) Assignment may be interchanged.

Table 5; additionally, 164.75 (*s*, C=O); 133.32 (*s*); 132.47 (*d*); 128.48 (2*d*); 127.72 (2*d*); 114.17 (*s*, Me_2C); 27.18, 25.41 (2*q*, Me_2C); 17.85 (*q*, $(Me_2CH)_3Si$); 11.84 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 598.3060 (100, $[M+H]^+$, $C_{30}H_{44}N_5O_6Si^+$; calc. 598.3062), 620.2873 (60, $[M+Na]^+$, $C_{30}H_{43}N_5NaO_6Si^+$; calc. 620.2883). Anal. calc. for $C_{30}H_{43}N_5O_6Si$ (597.79): C 60.28, H 7.25, N 11.72: found: C 60.37, H 7.39, N 11.35.

N^6*-Benzoyl-8-[[(bis(4-methoxyphenyl)](phenyl)methyl]-2′,3′*-O-*isopropylidene-5′*-O-*(triisopropylsilyl)-adenosine* (**8**). A soln. of **7** (2.00 g, 3.28 mmol), EtN^iPr_2 (1.13 ml, 6.56 mmol), and DMAP (0.041 g, 0.33 mmol) in CH_2Cl_2 (30 ml) was cooled to 0°, treated with DMTrCl (2.27 g, 6.56 mmol), stirred at 50° for 3 h, cooled to r.t., washed with H_2O (3 × 10 ml), brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (180 g); AcOEt/cyclohexane 2:1) gave **8** (2.78 g, 94%). Yellow foam. R_f (AcOEt/cyclohexane 2:1) 0.36. M.p. 137–139° (dec.).

$[\alpha]_D^{25} = -16.6$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3408*w*, 3064*w*, 3014*m*, 2961*m*, 2944*m*, 2867*m*, 1709*m*, 1613*s*, 1589*m*, 1510*s*, 1463*s*, 1253*s*, 1177*m*, 1094*s*, 1071*s*, 1035*m*, 883*w*, 829*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 9.08 (br. *s*, NH); 8.05–8.00 (*m*, 2 arom. H); 7.65–7.19 (*m*, 12 arom. H); 6.87–6.80 (*m*, 4 arom. H); 3.77 (*s*, 2 MeO); 1.51, 1.39 (2*s*, Me_2C); 1.05–0.95 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 164.31 (*s*, C=O); 158.57 (2*s*); 143.80 (*s*); 134.86 (2*s*); 133.84 (*s*); 132.57 (*d*); 130.08 (4*d*); 128.76 (2*d*); 128.01 (2*d*); 127.89 (2*d*); 127.70 (2*d*); 126.69 (*d*); 113.94 (*s*, Me_2C); 113.22 (4*d*); 87.82 (*s*, Ph_3C); 55.24 (*q*, 2 MeO); 27.35, 25.66 (2*q*, Me_2C); 17.96 (*q*, $(Me_2CH)_3Si$); 11.96 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 303 (65, $(MeO_2)Ph_3C$), 618 (100), 922.4173 (86, $[M+Na]^+$, $C_{51}H_{61}N_5NaO_8Si^+$; calc. 922.4189).

N^6-*Benzoyl-8-{[bis(4-methoxyphenyl)](phenyl)methyl}-2′,3′*-O-*isopropylideneadenosine* (**9**). A soln. of **8** (2.00 g, 2.20 mmol) in THF (35 ml) was treated dropwise with 1M $Bu_4NF \cdot 3\,H_2O$ in THF (4.4 ml, 4.40 mmol) and stirred at 23° for 4 h. Evaporation and FC (silica gel (180 g); AcOEt/cyclohexane 2:1) gave **9** (1.46 g, 89%). White solid. R_f (AcOEt) 0.38. M.p. 186–188°. $[\alpha]_D^{25} = -46.5$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3611*w*, 3407*w*, 3287*w* (br.), 3067*w*, 3015*m*, 2960*w*, 2939*w*, 2874*w*, 2840*w*, 1711*m*, 1612*s*, 1592*m*, 1510*s*, 1463*m*, 1430*m*, 1253*s*, 1178*m*, 1082*s*, 1036*m*, 829*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 9.23 (br. *s*, NH); 8.04–8.00 (*m*, 2 arom. H); 7.63–7.19 (*m*, 12 arom. H); 6.85–6.80 (*m*, 4 arom. H); 5.80 (br. *d*, $J = 1.8$, 10.9, HO–C(5′)); 3.77 (*s*, 2 MeO); 1.37, 1.32 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 164.30 (*s*, C=O); 158.58 (2*s*); 143.78 (*s*); 134.81 (*s*); 134.77 (*s*); 133.55 (*s*); 132.66 (*d*); 130.01 (4*d*); 128.71 (2*d*); 127.93 (2*d*); 127.89 (2*d*); 127.75 (2*d*); 126.98 (*d*); 114.03 (*s*, Me_2C); 113.22 (4*d*); 87.94 (*s*, Ar_3C); 55.22 (*q*, 2 MeO); 27.61, 25.36 (2*q*, Me_2C). HR-MALDI-MS: 744.3034 (3, $[M+H]^+$, $C_{42}H_{42}N_5O_8^+$; calc. 744.3034), 766.2840 (100, $[M+Na]^+$, $C_{42}H_{41}N_5NaO_8^+$; calc. 766.2855).

8-(Hydroxymethyl)-2′,3′-O-*isopropylidene-5′*-O-*(triisopropylsilyl)adenosine* (**10**). A soln. of **7** (500 mg, 0.83 mmol) in MeOH (16.8 ml) was treated at 23° with 25% aq. NH_3 (12.8 ml, 83 mmol), warmed to 60°, stirred for 2 h, cooled to r.t., and evaporated. FC (silica gel (50 g); CH_2Cl_2/MeOH 9:1) gave **10** (392 mg, 96%). White solid. R_f (AcOEt) 0.25. M.p. 143–146°. $[\alpha]_D^{25} = -15.3$ ($c = 1$, $CHCl_3$). UV (MeOH): 261 (12500). IR ($CHCl_3$): 3524*w*, 3495*w*, 3413*w* (br.), 3016*m*, 2961*m*, 2945*m*, 2867*m*, 1635*s*, 1592*w*, 1462*w*, 1375*m*, 1239*w*, 1087*s*, 883*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 6.12 (br. *s*, NH_2); 5.85 (br. *s*, OH); 1.61, 1.40 (2*s*, Me_2C); 1.00–0.90 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 114.24 (*s*, Me_2C); 27.13, 25.34 (2*q*, Me_2C); 17.78 (*q*, $(Me_2CH)_3Si$); 11.79 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 494.2801 (60, $[M+H]^+$, $C_{23}H_{40}N_5O_5Si^+$; calc. 494.2799), 516.2620 (100, $[M+Na]^+$, $C_{23}H_{39}N_5NaO_5Si^+$; calc. 516.2620).

8-(Hydroxymethyl)-2′,3′-O-*isopropylideneadenosine* (**11**). A soln. of **10** (300 mg, 0.60 mmol) and AcOEt (34 µl, 0.60 mmol) in THF (4.8 ml) was treated dropwise with 1M $Bu_4NF \cdot 3\,H_2O$ in THF (1.19 ml, 1.19 mmol), stirred at 23° for 3 h, and evaporated. A soln. of the residue in CH_2Cl_2 (20 ml) was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (25 g); AcOEt/MeOH 9:1) gave **11** (176 mg, 87%). White solid. Recrystallization in AcOEt gave colourless crystals submitted for X-ray analysis. R_f (AcOEt/MeOH 9:1) 0.17. M.p. 212–214°. $[\alpha]_D^{25} = -40.8$ ($c = 1$, $CHCl_3$). UV (MeOH): 259 (9300). IR ($CHCl_3$): 3526*w*, 3412*w*, 3218*w* (br.), 3017*m*, 2994*w*, 2942*w*, 2870*w*, 1637*s*, 1592*w*, 1476*w*, 1454*w*, 1420*w*, 1375*m*, 1103*m*, 1082*m*, 852*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 6.65 (br. *d*, $J = 10.3$, HO–C(5′)); 6.48 (br. *s*, NH_2); 5.78 (br. *s*, *H*OCH$_2$–C(8)); 1.64, 1.37 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 113.99 (*s*, Me_2C); 27.68, 25.47 (2*q*, Me_2C). HR-MALDI-MS: 338.1464 (100, $[M+H]^+$, $C_{14}H_{19}N_5O_5^+$; calc. 338.1465), 360.1282 (50, $[M+Na]^+$, $C_{14}H_{19}N_5NaO_5^+$; calc. 360.1286). Anal. calc. for $C_{14}H_{19}N_5O_5$ (337.33): C 49.85, H 5.68, N 20.76, O 23.71: found: C 50.09, H 5.76, N 20.97, O 23.50.

8-(Hydroxymethyl)adenosine (**12**). A suspension of **11** (100 mg, 0.29 mmol) in 80% aq. HCO_2H soln. (2.5 ml) was stirred for 6 h at 0° and evaporated. The residue was dissolved in H_2O (2 ml), adsorbed onto (silica gel (1.0 g) and taken to dryness. FC (silica gel (15 g); AcOEt/MeOH/H_2O 7:2:1) gave **12** (79 mg, 92%). White solid. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.28. M.p. >200° (dec.). $[\alpha]_D^{25} = -41.7$ ($c = 0.33$, MeOH/H_2O 2:1). UV (MeOH): 259 (8300). IR (ATR): 3421*m*, 3317*m*, 3162*m* (br.), 2925*m*, 2852*m*, 1654*s*, 1607*m*, 1594*m*, 1491*w*, 1454*w*, 1423*w*, 1374*w*, 1323*m*, 1312*m*, 1256*w*, 1124*w*, 1067*s*, 987*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 4*. ^{13}C-NMR (75 MHz, (D_6)DMSO): see *Table 5*. HR-MALDI-MS: 298.1140 (32, $[M+H]^+$, $C_{11}H_{16}N_5O_5^+$; calc. 298.1152), 320.0954 (3, $[M+Na]^+$, $C_{11}H_{15}N_5NaO_5^+$; calc. 320.0973).

6-(Hydroxymethyl)-2′,3′-O-*isopropylidene-5′*-O-*(triisopropylsilyl)uridine* (**15**). A soln. of $^iPr_2NH$ (53 ml, 370.7 mmol) in THF (210 ml) was cooled to −78°, treated dropwise with 1.6M BuLi in hexane (232 ml, 370.7 mmol), stirred for 15 min, warmed to 0°, stirred for 15 min, cooled to −78°, treated dropwise with a soln. of **14** [1] (33.0 g, 74.15 mmol) in THF (300 ml) over 10 min, stirred for 1 h, treated with DMF (144 ml, 1854 mmol), stirred for 2.5 h, treated with AcOH (54 ml), allowed to warm to 23°, diluted with EtOH (524 ml), treated slowly with $NaBH_4$ (8.7 g, 222 mmol), stirred for 25 min, and evaporated. A soln. of the residue in CH_2Cl_2 (500 ml) was washed with H_2O (2 × 250 ml) and brine (1 × 250 ml), dried ($MgSO_4$), and evaporated. FC

(silica gel (2×500 g); AcOEt/cyclohexane 1:1 → AcOEt) gave **15** (24.48 g, 70%). White solid. R_f (AcOEt/cyclohexane 2:1) 0.23. M.p. 77–79°. $[\alpha]_D^{25} = 21.5$ ($c = 1$, $CHCl_3$). UV (MeOH): 259 (9300). IR ($CHCl_3$): 3606*w*, 3391*w* (br.), 3031*w*, 2946*m*, 2894*w*, 2869*m*, 1698*s* (br.), 1627*w*, 1463*m*, 1383*m*, 1159*w*, 1135*w*, 1094*m*, 1067*m*, 974*w*, 881*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 9.39 (br. *s*, H–N(3)); 3.53 (br. *s*, *H*OCH$_2$–C(6)); 1.55, 1.33 (2*s*, Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 113.67 (*s*, Me_2C); 27.24, 25.35 (2*q*, *Me*$_2$C); 17.90 (*q*, $(Me_2CH)_3Si$); 11.97 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 493.2355 (100, $[M+Na]^+$, $C_{22}H_{38}N_2NaO_7Si^+$; calc. 493.2348). Anal. calc. for $C_{22}H_{38}N_2O_7Si$ (470.63): C 56.15, H 8.14, N 5.95: found: C 56.15, H 8.24, N 6.00.

Table 6. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Uridine Monomers* **13**–**18** *and* **20**–**22** *in $CDCl_3$, and* **19** *in CD_3OD*

	13[a])	**14** [1]	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**
H–C(1′)	5.56	5.99	5.81	5.60	5.51	5.77	5.47	5.88	5.82	5.86
H–C(2′)	5.05	4.69	5.19	5.19	5.22	5.24	4.74	5.23	5.25	5.28
H–C(3′)	4.97	4.85	4.83	4.78	5.00	4.96	4.31	4.82	4.84	4.85
H–C(4′)	4.30	4.27	4.18	4.07	4.12	4.23	3.88	4.19	4.19	4.21
H_a–C(5′)	3.93	4.00	3.94	3.86	3.86	3.89	3.79	3.87	3.87	3.87
H_b–C(5′)	3.81	3.88	3.89	3.80	3.75	3.82	3.66	3.85	3.85	3.86
H–C(5)	5.67	5.67	5.80	5.76	5.81	5.82	5.88	5.58	5.82	5.80
H–C(6)	7.68	7.68	–	–	–	–	–	–	–	–
CH_a–C(6)	–	–	4.57	4.03	4.04	4.55	4.53	5.12	4.44	4.26
CH_b–C(6)	–	–	4.50	3.97	3.94	4.46	4.47	5.04	4.32	4.17
J(1′,2′)	3.1	2.8	1.2	1.2	2.5	2.2	4.1	1.2	1.2	1.2
J(2′,3′)	6.5	6.2	6.3	6.3	6.6	6.5	6.2	6.5	6.2	6.3
J(3′,4′)	3.4	3.4	4.5	4.5	3.9	4.4	6.2	4.4	4.3	4.4
J(4′,5′a)	2.3	2.5	5.7	5.7	3.1	2.8	3.1	5.3	5.4	5.3
J(4′,5′b)	3.6	3.4	6.9	6.9	4.0	5.3	5.6	7.2	5.1	7.2
J(5′a,5′b)	12.3	11.2	11.1	[b])	12.1	12.5	11.8	11.2	10.9	12.1
J(5′a,OH)	3.6	–	–	–	3.1	[b])	–	–	–	–
J(5′b,OH)	7.5	–	–	–	7.8	[b])	–	–	–	–
J(5,6)	8.1	8.1	–	–	–	–	–	–	–	–
J(5,CH_2)	–	–	< 1.0	< 1.0	< 1.0	< 1.0	1.0	< 1.0	< 1.0	< 1.0
J(H_a,H_b)	–	–	14.9	12.9	12.9	14.5	15.0	13.4	13.2	11.5

[a]) Sparingly soluble in $CDCl_3$; spectrum of a third-saturated solution. Additional signals: 8.20 (br. *s*, NH); 2.62 (*dd*, $J = 3.6$, 7.5 HO–C(5′)). [b]) Not determined.

Table 7. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Uridine Monomers* **13** *in CD_3OD,* **14**–**18** *and* **20**–**22** *in $CDCl_3$, and* **19** *in (D_6)DMSO*

	13 [1]	**14** [1]	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**
C(1′)	94.4	91.7	91.06	91.95	92.22	91.44	92.06	91.96	91.68	91.79
C(2′)	86.1	85.4	84.05	84.10	83.21	83.66	71.77	84.00	84.16	84.18
C(3′)	82.4	80.0	81.76	82.14	80.26	80.47	70.24	81.85	81.83	81.89
C(4′)	88.6	86.9	89.51	89.44	87.28	87.94	85.12	89.67	89.82	89.90
C(5′)	63.3	63.5	64.34	64.45	62.72	62.55	62.52	64.25	64.29	64.39
C(2)	166.6	163.7	163.84	163.32	162.70	163.74	164.68	162.46	162.66	162.14
C(4)	152.5	150.4	150.32	150.33	151.08	150.95	151.28	149.98	150.26	150.15
C(5)	102.9	102.5	101.09	102.35	103.04	101.39	99.86	104.52	104.58	104.52
C(6)	144.2	140.9	155.43	152.80	152.40	155.63	157.56	147.74	150.54	151.05
CH_2–C(6)	–	–	60.55	62.07	62.13	60.54	59.53	38.52	41.06	26.41

6-{[Bis(4'-methoxyphenyl)](phenyl)methyl}-2',3'-O-*isopropylidene-5'*-O-*(triisopropylsilyl)uridine* (**16**). A soln. of **15** (10.0 g, 20.82 mmol), EtN^iPr_2 (7.2 ml, 41.65 mmol), and DMAP (0.26 g, 2.08 mmol) in CH_2Cl_2 (133 ml) was cooled to 0°, treated with DMTrCl (14.55 g, 41.65 mmol), stirred at 40° for 1 h, washed with H_2O (3 × 60 ml) and brine (1 × 60 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (400 g); AcOEt/cyclohexane 1:2) gave **16** (15.21 g, 95%). Yellow foam. R_f (AcOEt/cyclohexane 1:2) 0.21. M.p. 65–68° (dec.). $[\alpha]_D^{25} = -2.0$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3393*w*, 3064*w*, 3011*m*, 2944*m*, 2868*w*, 2840*w*, 1697*s*, 1609*m*, 1585*w*, 1510*s*, 1465*m*, 1384*m*, 1251*s*, 1179*m*, 1067*m*, 1038*m*, 978*w*, 882*w*, 832*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 8.86 (br. *s*, H–N(3)); 7.50–7.20 (*m*, 9 arom. H); 6.90–6.80 (*m*, 4 arom. H); 3.80 (*s*, 2 MeO); 1.43, 1.31 (2*s*, Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 158.66 (2*s*); 143.55 (*s*); 134.64, 134.52 (2*s*); 129.86 (4*d*); 127.91 (2*d*); 127.84 (2*d*); 127.11 (*d*); 113.29 (*s*, Me_2C); 113.29, 113.24 (4*d*); 87.92 (*s*, Ar_3C); 55.23 (*q*, 2 MeO); 27.27, 25.54 (2*q*, Me_2C); 17.95 (*q*, $(Me_2CH)_3Si$); 12.01 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 795.3658 ($[M+Na]^+$, $C_{43}H_{56}N_2NaO_9Si^+$; calc. 795.3655).

6-{[Bis(4-methoxyphenyl)](phenyl)methyl}-2',3'-O-*isopropylideneuridine* (**17**). A soln. of **16** (5.00 g, 6.4 mmol) in THF (52 ml) was treated dropwise with 1M $Bu_4NF \cdot 3\,H_2O$ in THF (12.8 ml, 12.8 mmol) and stirred at 23° for 2 h. Evaporation and FC (silica gel (100 g); AcOEt/cyclohexane 1:1) gave **17** (3.51 g, 89%). White solid. R_f (AcOEt/cyclohexane 1:1) 0.29. M.p. 132–135°. $[\alpha]_D^{25} = -21.6$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3608*w*, 3480*w* (br.), 3390*w*, 3030*w*, 3012*w*, 2937*w*, 2839*w*, 1695*s* (br.), 1608*m*, 1584*w*, 1510*m*, 1457*w*, 1385*w*, 1251*m*, 1177*m*, 1070*w*, 1035*m*, 977*w*, 835*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 9.32 (br. *s*, H–N(3)); 7.50–7.20 (*m*, 9 arom. H); 6.90–6.80 (*m*, 4 arom. H); 3.80 (*s*, 2 MeO); 3.07 (*dd*, $J = 3.1$, 7.8, HO–C(5')); 1.37, 1.29 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 158.70 (2*s*); 143.50 (*s*); 134.55, 134.44 (2*s*); 129.89 (4*d*); 127.95 (2*d*); 127.80 (2*d*); 127.16 (*d*); 113.94 (*s*, Me_2C); 113.33, 113.28 (4*d*); 88.00 (*s*, Ar_3C); 55.26 (*q*, 2 MeO); 27.29, 25.33 (2*q*, Me_2C). HR-MALDI-MS: 639.2305 ($[M+Na]^+$, $C_{34}H_{36}N_2NaO_9^+$; calc. 639.2321).

6-(Hydroxymethyl)-2',3'-O-*isopropylideneuridine* (**18**). A soln. of **15** (400 mg, 0.84 mmol) and AcOEt (97 µl, 1.68 mmol) in THF (6.8 ml) was treated dropwise with 1M $Bu_4NF \cdot 3\,H_2O$ in THF (1.68 ml, 1.68 mmol), stirred at 23° for 3 h, and evaporated. A soln. of the residue in CH_2Cl_2 (20 ml) was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (25 g); AcOEt) gave **18** (235 mg, 89%). White solid. Recrystallization in AcOEt gave colourless crystals submitted for X-ray analysis. R_f (AcOEt) 0.22. M.p. 192–195°. $[\alpha]_D^{25} = -6.7$ ($c = 0.5$, $CHCl_3$). UV (MeOH): 258 (8300). IR ($CHCl_3$): 3603*w*, 3400*w* (sh), 3388*w* (br.), 3019*s*, 2931*w*, 2857*w*, 1699*s* (br.), 1627*w*, 1602*w*, 1457*w*, 1384*w*, 1101*w*, 1068*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 9.26 (br. *s*, H–N(3)); 3.45–3.30 (br. *s*, 2 OH); 1.56, 1.34 (2*s*, Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 114.20 (*s*, Me_2C); 27.29, 25.34 (2*q*, Me_2C). HR-MALDI-MS: 337.1003 (28, $[M+Na]^+$, $C_{13}H_{18}N_2NaO_7^+$; calc. 337.1014). Anal. calc. for $C_{13}H_{18}N_2O_7$ (314.29): C 49.68, H 5.77, N 8.91, O 35.63: found: C 49.58, H 5.85, N 8.92, O 35.62.

6-(Hydroxymethyl)uridine (**19**). An 80% aq. soln. of HCO_2H (2.5 ml) was treated with **18** (100 mg, 0.31 mmol), stirred at 0° for 14 h, and evaporated. A soln. of the residue in H_2O (2 ml) was adsorbed onto silica gel (1.0 g) and evaporated. FC (silica gel (15 g); AcOEt/MeOH/H_2O 7:2:1) gave **19** (77 mg, 90%). White solid. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.31. M.p. 173–175°. $[\alpha]_D^{25} = -33.1$ ($c = 0.33$, MeOH/H_2O 2:1). UV (MeOH): 251 (7900). IR (ATR): 3364*m*, 3299*m* (br.), 3126*w*, 2919*w*, 2857*w*, 1719*s*, 1685*s*, 1655*s*, 1620*m*, 1481*w*, 1447*w*, 1390*m*, 1339*m*, 1270*m*, 1102*s*, 1072*s*, 1031*s*, 983*m*, 940*m*, 889*m*, 828*s*, 764*s*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 6*. ^{13}C-NMR (75 MHz, CD_3OD): see *Table 7*.

2',3'-O-*Isopropylidene-6-{[(methylsulfonyl)oxy]methyl}-5'*-O-*(triisopropylsilyl)uridine* (**20**). A soln. of **15** (250 mg, 0.53 mmol) and Et_3N (0.3 ml) in CH_2Cl_2 (10 ml) was cooled to 0°, treated with Ms_2O (193 mg, 1.06 mmol), stirred for 1 h, washed with H_2O (2 × 25 ml) and brine (1 × 25 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (5.0 g); AcOEt/cyclohexane 1:1) gave **20** (263 mg, 90%). White foam. R_f (AcOEt) 0.58. M.p. 51–53°. $[\alpha]_D^{25} = 9.3$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3384*w*, 3084*w*, 2944*m*, 2891*m*, 2867*m*, 1703*s*, 1459*m*, 1376*m*, 1354*m*, 1178*w*, 1090*m*, 1067*m*, 965*w*, 882*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 9.75 (br. *s*, H–N(3)); 3.15 (*s*, MsO); 1.53, 1.33 (2*s*, Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 113.82 (*s*, Me_2C); 38.52 (*q*, MsO); 27.24, 25.46 (2*q*, Me_2C); 17.95 (*q*, $(Me_2CH)_3Si$); 11.97 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 571.2117 (100, $[M+Na]^+$, $C_{23}H_{40}N_2NaO_9SSi^+$; calc. 571.2124).

6-(Chloromethyl)-2',3'-O-*isopropylidene-5'*-O-*(triisopropylsilyl)uridine* (**21**). A soln. of **15** (982 mg, 2.07 mmol) and DMAP (24 mg, 0.2 mmol) in pyridine (16.7 ml) was cooled to 0°, treated dropwise with MsCl (0.33 ml, 4.13 mmol), warmed to 23°, stirred for 1 h, treated with CH_2Cl_2 (50 ml), washed with H_2O (2 × 25 ml) and brine (1 × 25 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (25 g); AcOEt) gave **21** (952 mg, 95%). Yellow foam. R_f (AcOEt) 0.66. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 10.18 (br. *s*, H–N(3));

1.54, 1.33 (2*s*, Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 113.64 (*s*, Me_2C); 27.28, 25.39 (2*q*, Me_2C); 17.91 (*q*, $(Me_2CH)_3Si$); 11.99 (*d*, $(Me_2CH)_3Si$).

*6-(Bromomethyl)-2′,3′-*O*-isopropylidene-5′-*O*-(triisopropylsilyl)uridine* (**22**). A soln. of **15** (500 mg, 1.04 mmol) and CaH_2 (90 mg, 2.08 mmol) in Et_2O (11 ml) was cooled to 0°, treated with PBr_3 (160 µl, 1.26 mmol), stirred in the dark for 2 h, treated with H_2O (10 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The org. layer was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (15 g); cyclohexane/AcOEt 2:1) gave **22** (370 mg, 67%). White solid. R_f (cyclohexane/AcOEt 2:1) 0.38. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 6*; additionally, 9.38 (br. *s*, H–N(3)); 1.56, 1.35 (2*s*, Me_2C); 1.10–0.98 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 113.68 (*s*, Me_2C); 27.34, 25.47 (2*q*, Me_2C); 17.99 (*q*, $(Me_2CH)_3Si$); 12.04 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 557.1485 (54, $[M+Na]^+$, $C_{22}H_{37}{}^{81}BrN_2NaO_6Si^+$; calc. 557.1481), 555.1504 (53, $[M+Na]^+$, $C_{22}H_{37}{}^{79}BrN_2NaO_6Si^+$; calc. 555.1502).

*2′,3′-*O*-Isopropylidene-5′-*O*-(triisopropylsilyl)uridine-6-methyl-(6^1→5′)-*N^6*-benzoyl-2′,3′-*O*-isopropylideneadenosine* (**23**). A soln. of **5** (358 mg, 0.86 mmol) in DMF (6.7 ml) was cooled to 0°, treated with 60% NaH in oil (172 mg, 4.30 mmol), stirred for 30 min, treated dropwise with a soln. of **21** (510 mg, 0.98 mmol) in THF (7.0 ml), stirred for 2 h, treated with NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The org. layer was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (100 g); AcOEt/cyclohexane 1:1 → AcOEt) gave **23** (459 mg, 62%). White solid. R_f (AcOEt) 0.22. M.p. 133–136°. $[\alpha]_D^{25} = +26.5$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3390*w*, 2996*m*, 2944*m*, 2867*m*, 1704*s*, 1610*s*, 1586*m*, 1516*w*, 1480*w*, 1456*s*, 1383*s*, 1157*m*, 1092*s*, 1072*s*, 881*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 8*; additionally, 11.14 (br. *s*, H–N(3/II)); 10.06 (br. *s*, HN–C(6/I)); 8.14–8.12 (*m*, 2 arom. H); 7.54–7.40 (*m*, 3 arom. H); 1.63, 1.51, 1.44, 1.33 (4*s*, 2 Me_2C); 1.10–0.95 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 165.28 (*s*, C=O/I); 133.03 (*s*); 132.48 (*d*); 128.49 (2*d*); 128.37 (2*d*); 113.77, 113.45 (2*s*, 2 Me_2C); 27.33, 27.17, 25.78, 25.52 (4*q*, 2 Me_2C); 17.91 (*q*, $(Me_2CH)_3Si$); 11.95 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 886.3772 (100, $[M+Na]^+$, $C_{42}H_{57}N_7NaO_{11}Si^+$; calc. 886.3785), 864.3985 (36, $[M+H]^+$, $C_{42}H_{58}N_7O_{11}Si^+$; calc. 864.3964).

*2′,3′-*O*-Isopropylidene-5′-*O*-(triisopropylsilyl)uridine-6-methyl-(6^1→5′)-2′,3′-*O*-isopropylideneadenosine* (**24**). A soln. of **23** (218 mg, 0.25 mmol) in MeOH (4.0 ml) was treated at 23° with 25% aq. NH_3 (3.85 ml, 25 mmol), stirred at 60° for 2 h, cooled to r.t., and evaporated. FC (silica gel (15 g); CH_2Cl_2/MeOH 9:1) gave **24** (187 mg, 99%). White solid. R_f (CH_2Cl_2/MeOH 9:1) 0.33. M.p. 126–129°. $[\alpha]_D^{25} = +49.5$ ($c = 1$, $CHCl_3$). UV (MeOH): 259 (23000). IR ($CHCl_3$): 3484*w*, 3185*w*, 2993*m*, 2944*m*, 2866*m*, 1717*s* (br.), 1642*s*, 1600*m*, 1471*m*, 1384*s*, 1158*m*, 1090*s*, 1048*m*, 881*m*, 833*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 8*; additionally, 13.53 (br. *s*, H–N(3/II)); 6.94 (br. *s*, H_2N–C(6/I)); 1.61, 1.54, 1.43, 1.37 (4*s*, 2 Me_2C); 1.01–0.93 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 113.52, 113.38 (2*s*, 2 Me_2C); 27.42, 27.19, 26.02, 25.65 (4*q*, 2 Me_2C); 17.89 (*q*, $(Me_2CH)_3Si$); 11.96 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 782.3509 (100, $[M+Na]^+$, $C_{35}H_{53}N_7NaO_{10}Si^+$; calc. 782.3523), 760.3699 (38, $[M+H]^+$, $C_{35}H_{54}N_7O_{10}Si^+$; calc. 760.3702).

*2′,3′-*O*-Isopropylideneuridine-6-methyl-(6^1→5′)-2′,3′-*O*-isopropylideneadenosine* (**25**). A soln. of **24** (220 mg, 0.29 mmol) in THF (2.3 ml) was treated with TBAF·3 H_2O (186 mg, 0.57 mmol), stirred at 23° for 3 h, and evaporated. FC (silica gel (50 g); CH_2Cl_2/MeOH 9:1) gave **25** (138 mg, 80%). White solid. R_f (CH_2Cl_2/MeOH 8:2) 0.51. M.p. 175–178°. UV (MeOH): 258 (19500). IR (ATR): 3338*w* (br.), 3265*w*, 3207*w* (br.), 2988*w*, 2925*w*, 2857*w*, 2810*w*, 1693*s* (br.), 1648*m*, 1601*m*, 1573*w*, 1474*w*, 1374*m*, 1209*s*, 1156*m*, 1090*s*, 1068*s*, 867*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 8*; additionally, 13.02 (br. *s*, H–N(3/II)); 6.82 (br. *s*, H_2N–C(6/I)); 1.62, 1.57, 1.44, 1.40 (4*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 9*; additionally, 114.90, 114.78 (2*s*, 2 Me_2C); 27.70, 27.50, 26.15, 25.79 (4*q*, 2 Me_2C). HR-MALDI-MS: 432.2 (100), 604.2360 (45, $[M+H]^+$, $C_{26}H_{34}N_7O_{10}^+$; calc. 604.2368), 626.2177 (21, $[M+Na]^+$, $C_{26}H_{33}N_7NaO_{10}^+$; calc. 626.2189).

Uridine-6-methyl-(6^1→5′)-adenosine (**26**). An 80% aq. soln. of HCO_2H (0.9 ml) was cooled to 0°, treated with **25** (24 mg, 0.04 mmol), stirred for 6 h, diluted with H_2O (5 ml), adsorbed onto silica gel (1.5 g), and dried. FC (silica gel (15 g); AcOEt/MeOH/H_2O 7:2:1) gave **26** (19 mg, 93%). White solid. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.32. M.p. 177–180° (dec.). IR (ATR): 3452*m*, 3408*m* (br.), 3282*m*, 3202*m* (br.), 3148*m*, 2963*w*, 2918*w*, 2882*w*, 2754*w* (br.), 2708*w*, 1886*w*, 1705*s*, 1673*s*, 1654*s*, 1607*m*, 1573*w*, 1473*w*, 1445*m*, 1419*m*, 1382*m*, 1300*m*, 1119*s*, 1102*m*, 1076*s*, 1045*s*, 854*m*, 767*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 8*; additionally, 11.36 (br. *s*, H–N(3/II)); 7.28 (br. *s*, H_2N–C(6/I)); 5.49 (*d*, $J = 6.0$, OH); 5.28 (*d*, $J = 4.8$, OH); 5.14 (*d*, $J = 5.1$, OH); 4.98 (*d*, $J = 6.3$, OH); 4.71 (*t*, $J = 5.7$, HO–C(5′/II)). ^{13}C-NMR (75 MHz, (D_6)DMSO): see *Table 9*. HR-MALDI-MS: 524.1730 (100, $[M+H]^+$, $C_{20}H_{26}N_7O_{10}^+$, calc. 524.1742), 546.1564 (80, $[M+Na]^+$, $C_{20}H_{25}N_7NaO_{10}^+$; calc. 546.1563).

*2′,3′-*O*-Isopropylidene-5′-*O*-(triisopropylsilyl)uridine-6-methyl-(6^1→5′)-*N^6*-benzoyl-8-[[bis(4-methoxyphenyl)](phenyl)methyl]-2′,3′-*O*-isopropylideneadenosine* (**27**). A soln. of **9** (647 mg, 0.86 mmol) in DMF (6.7 ml) was cooled to 0°, treated with 60% NaH in oil (103 mg, 2.58 mmol), stirred for 30 min, treated with a soln. of **21**

Table 8. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Dimers* **23**–**25** *and* **27**–**30** *in $CDCl_3$,* **26** *and* **31** *in (D_6)DMSO, and* **32** *in D_2O*

	23[a])	**24**[a])	**25**	**26**[b])	**27**[a])	**28**[a])	**29**	**30**[b])	**31**[b])	**32**
H–C(1′/I)	6.18	6.20	6.17	5.90	6.33	6.22	6.33	6.19	6.32	6.06
H–C(2′/I)	5.75	5.66	5.68	4.62	5.70	5.88	6.03	5.75	5.59	5.30
H–C(3′/I)	5.19	5.26	5.22	4.26	5.19	5.34	5.40	5.32	5.10	4.66
H–C(4′/I)	4.61	4.57	4.58	4.11	4.33	4.31	4.42	4.34	4.28	4.28
H_a–C(5′/I)	3.74	3.75	3.85	3.79	3.77	3.65	3.69	3.76	3.70	3.98
H_b–C(5′/I)	3.74	3.70	3.73	3.71	3.68	3.63	3.62	3.64	3.55	3.69
H–C(2/I)	8.79	8.38	8.37	8.27	8.81	8.37	8.29	8.34	8.12	8.11
H–C(8/I)	8.23	7.96	7.93	8.16	–	–	–	–	–	–
CH_a–C(8/I)	–	–	–	–	4.60	4.55	4.97	4.51	4.67	4.90
CH_b–C(8/I)	–	-	–	–	4.53	4.41	4.92	4.43	4.67	4.90
J(1′,2′)	1.6	1.1	1.0	5.1	2.1	1.3	< 1.0	1.2	2.2	5.3
J(2′,3′)	6.0	6.0	6.3	4.2	6.5	6.3	5.9	6.2	6.2	5.3
J(3′,4′)	2.1	2.3	2.2	3.9	4.2	3.8	3.3	3.7	3.5	4.8
J(4′,5′a)	3.0	2.8	3.3	4.0	5.4	5.3	4.6	5.7	5.6	5.3
J(4′,5′b)	3.0	2.7	2.7	4.0	4.8	4.9	3.4	4.5	5.6	2.2
J(5′a,5′b)	[c])	10.4	10.5	10.6	10.5	10.5	10.5	11.1	10.9	11.2
J(H_a,H_b/I)	–	–	–	–	12.1	11.8	15.6	11.8	[c])	9.7
H–C(1′/II)	5.57	5.67	5.46	5.39	5.66	5.75	5.69	5.63	5.68	5.41
H–C(2′/II)	5.16	5.28	5.26	4.52	5.21	5.27	5.40	5.29	5.18	4.63
H–C(3′/II)	4.71	4.83	5.03	4.11	4.81	4.87	4.83	5.09	4.73	4.33
H–C(4′/II)	4.12	4.17	4.22	3.71	4.14	4.15	4.16	4.13	3.93	3.89
H_a–C(5′/II)	3.78	3.82	3.84	3.60	3.84	3.85	3.84	3.83	3.55	3.82
H_b–C(5′/II)	3.76	3.82	3.84	3.48	3.80	3.83	3.84	3.77	3.47	3.77
H–C(5/II)	5.41	5.40	5.34	5.77	5.62	5.36	5.40	5.38	5.70	5.75
CH_a–C(6/II)	4.30	4.36	4.32	4.47	4.44	4.44	4.33	4.39	4.47	4.44
CH_b–C(6/II)	3.93	3.86	4.05	4.47	4.22	4.03	4.00	4.16	4.25	4.44
J(1′,2′)	1.0	< 1.0	1.2	3.9	< 1.0	< 1.0	< 1.0	1.9	< 1.0	3.1
J(2′,3′)	6.4	6.3	6.3	6.3	6.3	6.3	5.9	6.4	6.5	6.5
J(3′,4′)	4.3	4.4	4.5	5.1	4.5	4.5	4.7	4.5	4.7	6.8
J(4′,5′a)	5.4	6.4	4.2	3.3	5.3	5.4	6.2	2.4	6.0	4.7
J(4′,5′b)	6.6	6.4	4.2	5.4	7.0	7.1	6.2	3.6	6.0	2.8
J(5′a,5′b)	10.5	[c])	[c])	12.0	10.5	10.5	[c])	11.4	12.0	10.3
J(H_a,H_b/II)	12.3	11.8	12.5	13.5	13.9	13.4	12.5	13.7	13.4	9.7

[a]) Assignment based on a DQFCOSY.GP spectrum. [b]) Assignment based on selective homodecoupling experiments. [c]) Not determined.

(510 mg, 1.03 mmol) in THF (6.8 ml), stirred for 2 h, treated with NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The org. layer was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (113 g); AcOEt/cyclohexane 1:1) gave **27** (652 mg, 63%). White solid. R_f (AcOEt) 0.47. M.p. 124–126°. $[\alpha]_D^{25} = -2.6$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3391*w*, 3007*m*, 2943*m*, 2867*m*, 1703*s* (br.), 1612*s*, 1590*w*, 1509*s*, 1462*s*, 1427*m*, 1384*m*, 1157*m*, 1070*s*, 1036*m*, 882*m*, 831*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 8*; additionally, 10.10 (br. *s*, H–N(3/II)); 9.64 (br. *s*, HN–C(6/I)); 8.07–8.04 (*m*, 2 arom. H); 7.59–7.46 (*m*, 4 arom. H); 7.41–7.37 (*m*, 4 arom. H); 7.31–7.20 (*m*, 4 arom. H); 7.06–6.81 (*m*, 4 arom. H); 3.77 (*s*, 2 MeO); 1.54, 1.52, 1.40, 1.34 (4*s*, 2 Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 164.93 (*s*, C=O/I); 158.55 (2*s*); 143.81 (*s*); 134.82, 134.77 (2*s*); 133.39 (*s*); 132.52 (*d*); 130.07 (4*d*); 128.53 (2*d*); 128.15 (2*d*); 128.00 (2*d*); 127.84 (2*d*); 126.96 (*d*); 114.36, 113.46 (2*s*, 2 Me_2C); 113.20 (4*d*); 87.85 (*s*, Ar_3C); 55.22 (*q*, 2 MeO); 27.35, 27.35, 25.69, 25.55 (4*q*, 2 Me_2C); 17.96 (*q*, $(Me_2CH)_3Si$); 11.20 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 303 (100, $DMTr^+$), 1218.499 (10, $[M + Na]^+$, $C_{64}H_{77}N_7NaO_{14}Si^+$; calc. 1218.5198).

Table 9. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *for the Dimers* **23**, **24**, *and* **27**–**30** *in $CDCl_3$,* **25** *and* **31** *in CD_3OD,* **26** *in (D_6)DMSO, and* **32** *in D_2O*

	23[a])	**24**[a])	**25**	**26**	**27**[a])	**28**[a])	**29**	**30**	**31**	**32**
C(1′/I)	93.01	92.01	93.20	91.68	89.92	90.00	89.90	90.08	91.17	91.91
C(2′/I)	84.21	84.22	85.79	71.19	83.43	83.57	83.44	83.61	84.50	71.56
C(3′/I)	81.73	81.71	82.90	69.72	81.69	81.67	81.25	80.57	82.95	69.16
C(4′/I)	86.38	86.94	87.88	82.78	85.79	86.74	87.02	87.17	87.30	83.09
C(5′/I)	71.39	71.43	72.30	70.39	70.55	69.80	70.53	69.46	71.50	69.71
C(2/I)	151.80	152.82	153.86	152.52	151.75	151.91	152.04	151.81	153.42	151.97
C(4/I)	150.37	149.03	150.15	151.14	149.54	150.10	150.19	149.88	151.41	149.65
C(5/I)	124.18	119.09	120.10	118.88	122.76	118.45	117.60	118.41	118.91	117.31
C(6/I)	151.55	155.66	157.06	155.83	152.45	155.61	155.44	155.53	156.76	154.58
C(8/I)	141.77	138.55	140.90	139.19	151.75	148.81	151.87	148.84	152.95	152.48
CH_2–C(8/I)	–	–	–	–	59.60	59.27	57.14	59.14	58.41	56.56
C(1′/II)	91.87	92.01	92.68	87.24	91.37	91.39	91.69	91.38	92.83	88.48
C(2′/II)	84.21	84.42	85.79	73.22	84.12	84.37	84.29	84.08	85.74	71.66
C(3′/II)	82.09	82.33	83.11	70.39	82.04	82.26	82.13	81.69	83.07	69.88
C(4′/II)	89.94	89.96	90.55	84.71	89.51	89.65	89.73	88.10	90.30	83.09
C(5′/II)	64.34	64.52	63.74	61.95	64.32	64.50	64.44	62.87	63.79	61.37
C(2/II)	163.00	164.11	165.30	163.34	162.59	164.07	164.52	163.55	165.60	165.05
C(4/II)	150.02	149.15	152.18	149.29	150.39	150.24	150.30	150.13	152.90	151.15
C(5/II)	104.05	104.79	104.91	102.09	102.93	103.71	103.77	103.90	103.93	102.77
C(6/II)	149.50	151.02	152.49	151.61	151.06	150.74	150.99	151.61	152.52	151.97
CH_2–C(6/II)	69.06	69.49	70.08	67.94	68.62	68.08	69.04	68.92	69.86	68.33

[a]) Assignment based on a DQFCOSY.GP and a HSQC.GP spectrum.

*2′,3′-*O*-Isopropylidene-5′-*O*-(triisopropylsilyl)uridine-6-methyl-(6^1→5′)-8-{[bis(4-methoxyphenyl)](phenyl)methyl}-2′,3′-*O*-isopropylideneadenosine* (**28**). A soln. of **27** (439 mg, 0.33 mmol) in MeOH (6.8 ml) was treated at 23° with 25% aq. NH_3 (5.15 ml, 33 mmol), stirred at 60° for 2 h, cooled to r.t., and evaporated. FC (silica gel (110 g); AcOEt) gave **28** (384 mg, 97%). White solid. R_f (AcOEt) 0.36. M.p. 134–136°. $[\alpha]_D^{25} = +24.4$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3488*w*, 3185*w*, 2993*m*, 2943*m*, 2866*m*, 2840*w*, 1712*s*, 1636*m*, 1608*m*, 1509*s*, 1446*m*, 1383*m*, 1157*m*, 1068*s*, 1036*m*, 882*m*, 831*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): see *Table 8*; additionally, 13.09 (br. *s*, H–N(3/II)); 8.37–7.49 (*m*, 2 arom. H); 7.47–7.38 (*m*, 4 arom. H); 7.32–7.21 (*m*, 3 arom. H); 6.90 (br. *s*, H_2N–C(6/I)); 6.86–6.83 (*m*, 4 arom. H); 3.79 (*s*, 2 MeO); 1.55, 1.55, 1.42, 1.41 (4*s*, 2 Me_2C); 1.01–0.96 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 158.50 (2*s*); 144.00 (*s*); 135.08 (2*s*); 130.02 (4*d*); 128.10 (2*d*); 127.81 (2*d*); 126.90 (*d*); 113.59, 113.26 (2*s*, 2 Me_2C); 113.17 (4*d*); 87.50 (*s*, Ar_3C); 55.23 (*q*, 2 MeO); 27.36, 27.36, 25.76, 25.76 (4*q*, 2 Me_2C); 17.95 (*q*, $(Me_2CH)_3Si$); 11.99 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 303 (100, $DMTr^+$), 1114.492 (3, $[M+Na]^+$, $C_{57}H_{73}N_7NaO_{13}Si^+$; calc. 1114.4936). Anal. calc. for $C_{57}H_{73}N_7O_{13}Si$ (1092.33): C 62.68, H 6.74, N 8.98: found: C 62.88, H 6.94, N 8.82.

*2′,3′-*O*-Isopropylidene-5′-*O*-(triisopropylsilyl)uridine-6-methyl-(6^1→5′)-8-(hydroxymethyl)-2′,3′-*O*-isopropylideneadenosine* (**29**). A soln. of **28** (170 mg, 0.15 mmol) in $MeNO_2$ (0.4 ml) was treated with HCO_2H (0.1 ml, 2.60 mmol), stirred at 23° for 1.5 h, diluted with CH_2Cl_2 (10 ml), washed with sat. $NaHCO_3$ soln. (5 ml) and brine (2 × 5 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (80 g); AcOEt/MeOH 95:5) gave **29** (103 mg, 85%). White solid. R_f (CH_2Cl_2/MeOH 9:1) 0.34. M.p. 142–144°. $[\alpha]_D^{25} = +38.7$ ($c = 0.5$, $CHCl_3$). UV (MeOH): 260 (28500). IR ($CHCl_3$): 3484*w*, 3409*w*, 3335*w*, 3198*w* (br.), 3018*w*, 2995*w*, 2943*m*, 2894*w*, 2867*m*, 1702*s* (br.), 1641*m*, 1604*w*, 1447*m*, 1383*s*, 1157*m*, 1089*s*, 1070*s*, 882*m*, 866*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 8*; additionally, 13.33 (br. *s*, H–N(3/II)); 7.15 (br. *s*, H_2N–C(6/I)); 5.24 (br. *s*, $HOCH_2$–C(8/I); 1.61, 1.56, 1.42, 1.42 (4*s*, 2 Me_2C); 1.01–0.94 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 113.61, 113.39 (2*s*, 2 Me_2C); 27.33, 27.28, 25.67, 25.60 (4*q*, 2 Me_2C); 17.95 (*q*, $(Me_2CH)_3Si$); 11.99 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 790.3822 (35, $[M+H]^+$, $C_{36}H_{56}N_7O_{11}Si^+$, calc. 790.3808), 812.3629 (100, $[M+Na]^+$, $C_{36}H_{55}N_7NaO_{11}Si^+$; calc. 812.3629).

2′,3′-O-*Isopropylideneuridine-6-methyl-(6¹ → 5′)-8-[[bis(4-methoxyphenyl)](phenyl)methyl]-2′,3′*-O-*isopropylideneadenosine* (**30**). A soln. of **28** (165 mg, 0.16 mmol) in THF (1.2 ml) was treated with 1M TBAF·3 H_2O in THF (0.3 ml, 0.30 mmol), stirred at 23° for 4 h, and evaporated. FC (silica gel (50 g); AcOEt) gave **30** (114 mg, 81%). White solid. R_f (CH_2Cl_2/MeOH 9:1) 0.21. M.p. 143–147° (dec.). $[\alpha]_D^{25} = +8.9$ ($c = 0.5$, $CHCl_3$). IR ($CHCl_3$): 3486*w*, 3409*w*, 3330*w* (br.), 3192*w*, 3015*m*, 2958*w*, 2930*m*, 2856*w*, 2842*w*, 1704*s* (br.), 1637*m*, 1607*m*, 1509*m*, 1446*m*, 1383*m*, 1376*m*, 1300*w*, 1252*s*, 1177*m*, 1156*m*, 1103*m*, 1070*s*, 1038*m*, 832*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 8*; additionally, 13.43 (br. *s*, H–N(3/II)); 7.52–7.20 (*m*, 9 arom. H); 6.91 (br. *s*, H_2N–C(6/I)); 6.87–6.82 (*m*, 4 arom. H); 3.79 (*s*, 2 MeO); 1.55, 1.54, 1.42, 1.40 (4*s*, 2 Me_2C); HO–C(5′/II) hidden by the signals at 3.84–3.72. ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 9*; additionally, 158.52 (2*s*); 143.96 (*s*); 135.03 (2*s*); 130.06 (4*d*); 128.08 (2*d*); 127.85 (2*d*); 126.91 (*d*); 113.99, 113.67 (2*s*, Me_2C); 113.21 (4*d*); 87.54 (*s*, Ar_3C); 55.25 (*q*, 2 MeO); 27.40, 27.40, 25.85, 25.52 (4*q*, 2 *Me*$_2$C). HR-MALDI-MS: 303 (100, $DMTr^+$), 958.3604 (12, $[M+Na]^+$, $C_{48}H_{53}N_7NaO_{13}^+$; calc. 958.3601).

2′,3′-O-*Isopropylideneuridine-6-methyl-(6¹ → 5′)-8-(hydroxymethyl)-2′,3′*-O-*isopropylideneadenosine* (**31**). a) *From* **29**. A soln. of **29** (66 mg, 0.08 mmol) in THF (1.0 ml) was treated with 1M TBAF in THF (0.16 ml, 0.16 mmol), stirred at 23° for 4 h, and evaporated. FC (silica gel (25 g); AcOEt) gave **31** (41 mg, 81%).

b) *From* **30**. A soln. of **30** (90 mg, 0.10 mmol) in $MeNO_2$ (0.4 ml) was treated with HCO_2H (0.1 ml, 2.60 mmol), stirred at 23° for 1 h, diluted with CH_2Cl_2 (10 ml), washed with sat. $NaHCO_3$ soln. (5 ml) and brine (2 × 5 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (15 g); CH_2Cl_2/MeOH 9:1 → 8:2) gave **31** (64 mg, 86%). White solid. R_f (CH_2Cl_2/MeOH 9:1) 0.17. M.p. 176–179°. $[\alpha]_D^{25} = -31.0$ ($c = 1$, MeOH). UV (MeOH): 260 (20800). IR (ATR): 3333*w* (br.), 3198*w*, 2987*w*, 2924*w*, 2853*w*, 1685*s* (br.), 1644*m*, 1606*m*, 1577*w*, 1447*m*, 1374*m*, 1330*w*, 1300*w*, 1259*w*, 1211*m*, 1157*w*, 1065*s* (br.), 969*w*, 863*m*, 831*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see *Table 8*; additionally, 11.45 (br. *s*, H–N(3/II)); 7.30 (br. *s*, H_2N–C(6/I)); 5.79 (*t*, $J = 5.3$, *H*OCH$_2$–C(8/I)); 4.79 (*t*, $J = 5.9$, HO–C(5′/II)); 1.52, 1.44, 1.31, 1.26 (4*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 9*; additionally, 115.00, 114.76 (2*s*, 2 Me_2C); 27.71, 27.58, 25.92, 25.75 (4*q*, 2 *Me*$_2$C). HR-MALDI-MS: 462.2 (100), 634.2460 (49, $[M+H]^+$, $C_{27}H_{36}N_7O_{11}^+$; calc. 634.2474), 656.2289 (14, $[M+Na]^+$, $C_{27}H_{35}N_7NaO_{11}^+$; calc. 656.2295).

Uridine-6-methyl-(6¹ → 5′)-8-(hydroxymethyl)adenosine (**32**). An 80% aq. soln. of HCO_2H (1.25 ml) was cooled to 0°, treated with **31** (50 mg, 0.08 mmol), stirred for 8 h at 23°, diluted with H_2O (5 ml), adsorbed onto silica gel (0.5 g) and taken to dryness. FC (silica gel (15 g); AcOEt/MeOH/H_2O 7:2:1) gave **32** (39 mg, 89%). White solid. R_f (AcOEt/MeOH/H_2O 7:2:1) 0.27. M.p. 177–179° (dec.). $[\alpha]_D^{25} = -8.6$ ($c = 1$, H_2O). IR (ATR): 3322*s* (br.), 3192*s* (br.), 2935*m*, 2863*m*, 1653*s* (br.), 1578*m*, 1447*m*, 1388*m*, 1331*m*, 1294*m*, 1250*w*, 1102*s*, 1044*s*, 1023*s* (br.), 904*w*, 852*m*, 796*w*. ^{1}H-NMR (300 MHz, D_2O): see *Table 8*. ^{13}C-NMR (75 MHz, D_2O): see *Table 9*. HR-MALDI-MS: 554.1848 (13, $[M+H]^+$, $C_{21}H_{28}N_7O_{11}^+$; calc. 554.1848), 576.1668 (14, $[M+Na]^+$, $C_{21}H_{27}N_7NaO_{11}^+$; calc. 576.1669).

2′,3′-O-*Isopropylidene-5′*-O-*(triisopropylsilyl)uridine-6-methyl-(6¹ → 5′)-6-[[bis(4-methoxyphenyl)](phenyl)methyl]-2′,3′*-O-*isopropylideneuridine* (**33**). A soln. of **17** (196 mg, 0.31 mmol) in DMF (2.4 ml) was cooled to 0°, treated with 60% NaH in oil (37 mg, 0.94 mmol), stirred for 30 min, treated with a soln. of **22** (170 mg, 0.31 mmol) in THF (2.5 ml), stirred for 1 h, treated with NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The org. layer was washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (silica gel (30 g); AcOEt/cyclohexane 2:1) gave **33** (167 mg, 50%). Yellow solid. R_f (AcOEt) 0.44. M.p. 125–128°. IR ($CHCl_3$): 3389*w*, 3019*m*, 2941*m*, 2867*m*, 1698*s* (br.), 1608*w*, 1509*w*, 1456*w*, 1383*m*, 1252*m*, 1176*w*, 1156*w*, 1088*m*, 1069*m* (br.), 1036*w*, 880*w*, 833*w*. ^{1}H-NMR (300 MHz, $CDCl_3$, assignment based on selective homodecoupling experiments): 10.35 (*d*, $J = 1.9$, H–N(3/I)); 9.84 (*d*, $J = 2.2$, H–N(3/II)); 7.47–6.82 (*m*, 13 arom. H); 5.84 (*d*, $J = 1.9$, H–C(5/I)); 5.72 (*d*, $J = 2.2$, H–C(5/II)); 5.71 (br. *s*, H–C(1′/II)); 5.68 (br. *s*, H–C(1′/II)); 5.22 (br. *d*, $J = 6.5$, H–C(2′/I)); 5.19 (br. *d*, $J = 6.2$, H–C(2′/II)); 4.88 (*dd*, $J = 4.7, 6.5$, H–C(3′/I)); 4.82 (*dd*, $J = 4.4, 6.2$, H–C(3′/II)); 4.51, 4.34 (2*d*, $J = 14.3$, CH_2–C(6/II)); 4.19 (*dt*, $J = 4.7, 6.5$, H–C(4′/I)); 4.15 (*dt*, $J = 4.4, 6.5$, H–C(4′/II)); 3.02, 3.96 (2*d*, $J = 12.5$, CH_2–C(6/I)); 3.84 (*d*, $J = 6.5$, 2 H–C(5′/II)); 3.80 (*s*, 2 MeO); 3.80–3.72 (*m*, 2 H–C(5′/I)); 1.51, 1.44, 1.31, 1.31 (4*s*, 2 Me_2C); 1.10–1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): 163.43, 163.19 (2*s*, 2 C(2)); 158.67 (2*s*); 152.14, 151.64 (2*s*, 2 C(4)); 150.64, 150.33 (2*s*, 2 C(6)); 143.50 (*s*); 134.58, 134.44 (2*s*); 129.90 (4*d*); 127.90 (4*d*); 127.15 (*d*); 113.70, 113.35 (2*s*, 2 Me_2C); 113.29, 113.22 (4*d*); 103.18, 102.81 (2*d*, 2 C(5)); 92.11, 91.22 (2*d*, 2 C(1′)); 89.66 (*d*, C(4′/II)); 88.01 (*s*, Ar_3C); 87.42 (*d*, C(4′/I)); 84.43, 84.24 (2*d*, 2 C(2′)); 82.01, 81.68 (2*d*, 2 C(3′)); 70.77 (*t*, C(5′/I)); 68.59 (*t*, CH_2–C(6/II)); 64.46 (*t*, C(5′/II)); 62.33 (*t*, CH_2–C(6/I)); 55.25 (*q*, 2 MeO); 27.33, 27.23, 25.50 (2 C) (3*q*, 2 *Me*$_2$C); 17.97 (*q*, $(Me_2CH)_3Si$); 12.01 (*d*, $(Me_2CH)_3Si$). HR-MALDI-MS: 303 (100, $DMTr^+$), 1091.465 (5, $[M+Na]^+$, $C_{56}H_{72}N_4NaO_{15}Si^+$; calc. 1091.466).

N^6-*Benzoyl-2′,3′*-O-*isopropylidene-8-[(trichloroacetimidoxy)methyl]-5′*-O-*(triethylsilyl)adenosine* (**36**). A soln. of **34** (500 mg, 0.88 mmol) and trichloroacetonitrile (0.1 ml, 0.99 mmol) in CH_2Cl_2 (10 ml) was cooled to 0°, treated with DBU (0.15 ml, 0.99 mmol), stirred for 1 h, and evaporated. FC (silica gel (20 g); cyclohexane/AcOEt 8:2) gave **36** (530 mg, 86%). Yellow solid. R_f (AcOEt) 0.69. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 4*; additionally, 9.11 (br. *s*, HN–C(6)); 8.64 (br. *s*, HN=C); 8.05–7.90 (*m*, 2 arom. H); 7.64–7.40 (*m*, 3 arom. H); 1.60, 1.42 (2*s*, Me_2C); 0.84 (*t*, *J* = 7.4, (*Me*CH_2)$_3$Si); 0.50 (*q*, *J* = 7.4, (Me*C*H_2)$_3$Si). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 5*; additionally, 164.45 (*s*, C=O); 153.78 (*s*, C=NH); 133.66 (*s*); 132.77 (*d*); 128.87 (2*d*); 127.79 (2*d*); 114.26 (*s*, Me_2C); 91.30 (*s*, Cl_3C); 27.15, 25.41 (2*q*, *Me*$_2$C); 6.55 (*q*, (*Me*CH_2)$_3$Si)); 4.11 (*t*, (Me*C*H_2)$_3$Si)).

N^6-*Benzoyl-5′*-O-*[(dimethyl)(1,1,2-trimethylpropyl)silyl]-2′,3′*-O-*isopropylidene-8-[[(methylsulfonyl)oxy]-methyl]-5′*-O-*(thexyldimethylsilyl)-adenosine* (**37**). A soln. of **35** (100 mg, 0.17 mmol) and Et_3N (62 µl) in CH_2Cl_2 (1.2 ml) was cooled to 0°, treated with Ms_2O (60 mg, 3.4 mmol), stirred for 1 h, diluted with CH_2Cl_2 (10 ml), washed with H_2O (2 × 5 ml) and brine (1 × 5 ml), dried ($MgSO_4$), and evaporated to give **37** (95 mg, 85%). White foam. R_f (cyclohexane/AcOEt 1:1) 0.38. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 9.11 (br. *s*, NH); 8.05–7.90 (*m*, 2 arom. H); 7.64–7.40 (*m*, 3 arom. H); 3.12 (*s*, MsO); 1.62, 1.41 (2*s*, Me_2C); 1.57 (*sept.*, *J* = 6.9, Me_2CH); 0.83 (*d*, *J* = 6.9, *Me*$_2$CH); 0.78 (*s*, Me_2CSi); 0.00 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 164.48 (*s*, C=O); 133.41 (*s*); 132.91 (*d*); 128.89 (2*d*); 127.80 (2*d*); 114.53 (*s*, Me_2CO_2); 38.57 (*q*, MsO); 33.97 (*d*, Me_2CH); 27.15, 25.36 (2*q*, *Me*$_2$CO$_2$); 25.07 (*s*, Me_2CSi); 20.50 (*q*, *Me*$_2$CH); 18.47 (*q*, *Me*$_2$CSi); −3.33 (*q*, Me_2Si).

N^6-*Benzoyl-8-(chloromethyl)-5′*-O-*[(dimethyl)(1,1,2-trimethylpropyl)silyl]-2′,3′*-O-*isopropylideneadeno-sine* (**38**). A soln. of **35** (500 mg, 0.86 mmol) and Et_3N (0.24 ml) in CH_2Cl_2 (5 ml) was cooled to 0°, treated with MsCl (0.13 ml, 1.7 mmol), warmed to 23°, stirred for 1 h, treated with LiCl (360 mg, 8.57 mmol), stirred for 1 h, diluted with CH_2Cl_2 (25 ml), washed with H_2O (2 × 10 ml) and brine (1 × 10 ml), dried ($MgSO_4$), and evaporated. FC (AcOEt/cyclohexane 1:4) gave **38** (380 mg, 74%). White foam. R_f (cyclohexane/AcOEt 1:1) 0.47. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 4*; additionally, 8.94 (br. *s*, NH); 8.05–7.90 (*m*, 2 arom. H); 7.64–7.40 (*m*, 3 arom. H); 1.64, 1.42 (2*s*, Me_2C); 1.57 (*sept.*, *J* = 6.9, Me_2CH); 0.84 (*d*, *J* = 6.9, *Me*$_2$CH); 0.80 (*s*, Me_2CSi); 0.04 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 5*; additionally, 164.94 (*s*, C=O); 133.56 (*s*); 133.15 (*d*); 129.06 (2*d*); 128.22 (2*d*); 114.66 (*s*, Me_2CO_2); 34.25 (*d*, Me_2CH); 27.43, 25.63 (2*q*, *Me*$_2$CO$_2$); 25.47 (*s*, Me_2CSi); 20.46 (*q*, *Me*$_2$CH); 18.65 (*q*, *Me*$_2$CSi); −3.28 (*q*, Me_2Si). MALDI-MS: 602 (15, $[M+H]^+$), 624 (25, $[M+Na]^+$).

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