Oligonucleotide Analogues with Integrated Bases and Backbone

Part 18[1])

Synthesis and Association of Thiomethylene-Linked UU and AA Dimers

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The thiomethylene-linked U*[s]U$^{(*)}$ dimers **9**–**14** were synthesized by substitution of the 6-[(mesyloxy)methyl]uridine **6** by the thiolate derived from the uridine-5′-thioacetates **7** and **8** followed by *O*-deprotection. Similarly, the thiomethylene-linked A*[s]A$^{(*)}$ dimers **9**–**14** were obtained from the 8-(bromomethyl)adenosine **15** and the adenosine-5′-thioacetates **16** and **17**. The concentration dependence of both H–N(3) of the U*[s]U$^{(*)}$ dimers **9**–**14** evidences the formation of linear and cyclic duplexes, and of linear higher associates, C(8 or 6)CH_2OH and/or C(5′/II)OH groups favouring the formation of cyclic duplexes. The concentration dependence of the chemical shift for both H_2N–C(6) of the A*[s]A$^{(*)}$ dimers **18**–**23** evidences the formation of mainly linear associates. The heteroassociation of U*[s]U$^{(*)}$ to A*[s]A$^{(*)}$ dimers is stronger than the homoassociation of U*[s]U$^{(*)}$ dimers, as evidenced by diluting equimolar mixtures of **11**/**20** and **13**/**22**. A 1:1 stoichiometry of the heteroassociation is evidenced by a *Job*'s plot for **11**/**20**, and by mole ratio plots for **9**/**18**, **10**/**19**, **12**/**21**, **13**/**22**, and **14**/**23**.

Introduction. – In the context of the synthesis and pairing analysis of novel oligoribonucleotide analogues wherein the backbone of oligonucleotides is replaced by linking elements between nucleobases (ONIBs [2]), we have investigated the pairing of the self-complementary U*[s]A$^{(*)}$ and A*[s]U$^{(*)}$ dimers[2]) **1**–**5** (*Fig. 1*) [1]. The U*[s]A$^{(*)}$ alcohols **1** and **2** pair, *i.e.,* they form preferentially cyclic duplexes, whereas the fully protected analogues **3** only form linear duplexes and higher associates. In the A*[s]U$^{(*)}$ series, only the alcohol **4** forms (mainly) cyclic duplexes, whereas **5** leads predominantly to linear duplexes and higher associates, irrespectively of whether HO–C(5′/II) is protected or not.

Pairing of the self-complementary thiomethylene-brigded U*[s]A$^{(*)}$ and A*[s]U$^{(*)}$ dimers is sequence-dependent and favoured by unprotected OH groups, *viz.,* C(8)CH_2OH and/or C(5′/II)OH of U*[s]A$^{(*)}$, and C(6)CH_2OH of A*[s]U* dimers.

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1) For Part 17, see [1].

2) *Conventions for abbreviated notation:* The substitution at C(6) of pyrimidines and C(8) of purines is denoted by an asterisk (*); for example U* and A* for hydroxymethylated uridine and adenosine derivatives, respectively. U$^{(*)}$ and A$^{(*)}$ represent both unsubstituted and hydroxymethylated nucleobases. The moiety linking C(6)–CH_2 or C(8)–CH_2 (of unit II) and C(5′) (of unit I) is indicated in square brackets, *i.e.*, [c] for a C-atom, [o] for an O-, and [s] for a S-atom. The index y, e, or a indicates a triple, double, or single bond, respectively.

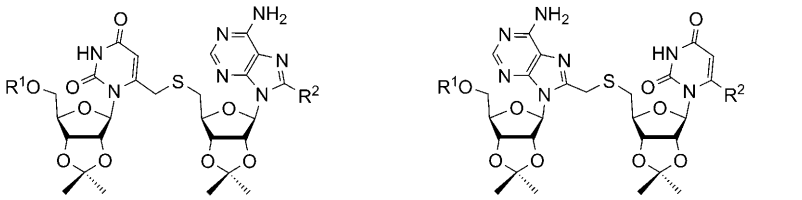


Fig. 1. *The self-complementary U*[s]A(*) dimers* **1** *and* **2**, *and the A*[s]U(*) dimer* **4** *prefer the formation of cyclic duplexes, whereas the U*[s]A(*) dimer* **3** *and the A*[s]U(*) dimer* **5** *form mainly linear duplexes and higher associates.* TDS = Thexyl(dimethyl)silyl (thexyl = 1,1,2-trimethylpropyl), MMTr = (monomethoxy)trityl = (4-methoxyphenyl)diphenylmethyl.

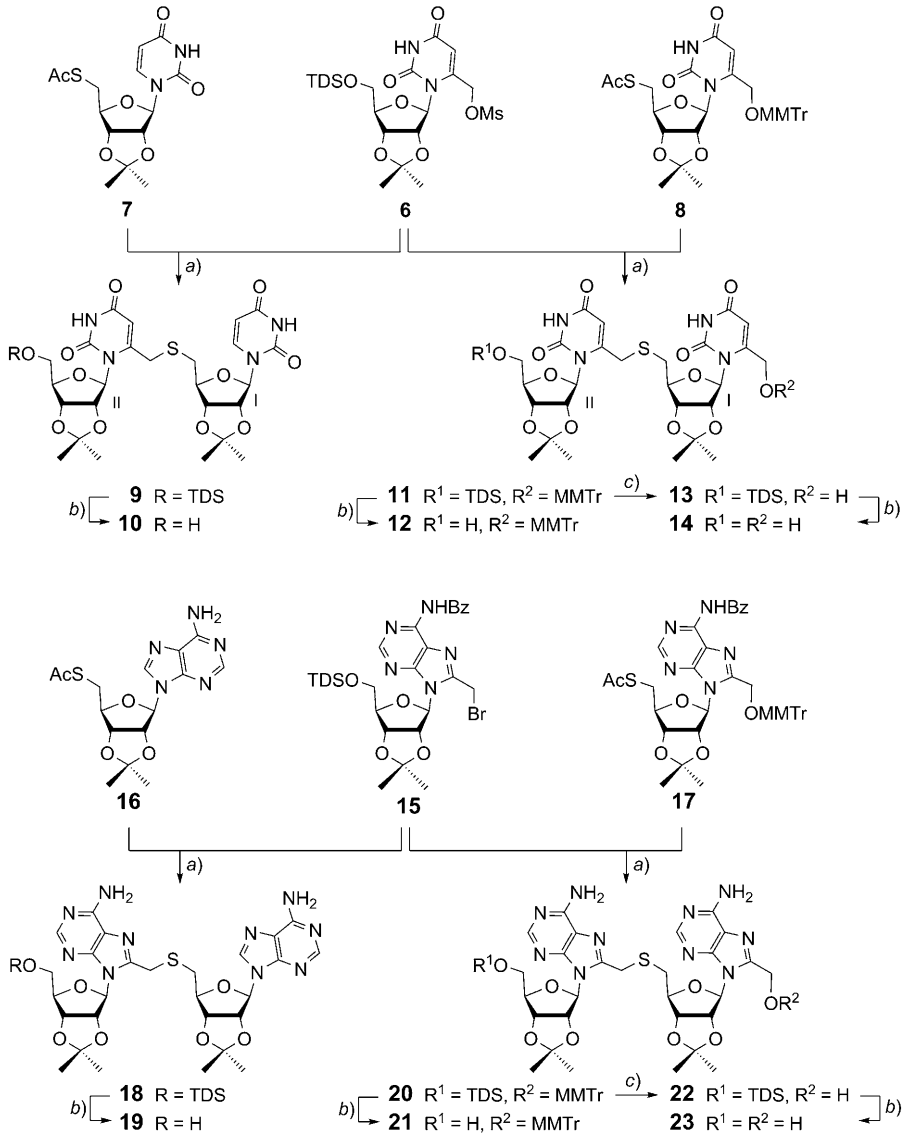
We wondered about the (hetero-)pairing of U*[s]U(*) and A*[s]A(*) dimers (the formation of cyclic duplexes) and the influence of unprotected OH substituents on pairing, and report the synthesis of U*[s]U(*) and A*[s]A(*) dimers, and the analysis of their association.

Results and Discussion. – 1. *Synthesis of the U*[s]U(*) and A*[s]A(*) Dimers.* These dimers were synthesized similarly as described for the U*[s]A(*) and A*[s]U(*) heterodimers [1]. Treatment of the thioacetates **7** [1] and **8** [1] with MeONa in MeOH generated the corresponding thiolates which reacted *in situ* with the protected *C(6)*-[(mesyloxy)methyl]uridine **6** [1] to form the U*[s]U(*) dimers **9** and **11** in 79 and 73% yield, respectively (*Scheme*). The analogous treatment with MeONa in MeOH of the A*[s]A(*) thioacetates **16** [1] and **17** [1] led to deacylation of both the thioacetyl and benzamido groups. The deacylation products reacted with the bromo derivatives **15** [1] to yield 79 and 84%, respectively, of the N^6-deprotected A*[s]A(*) dimers **18** and **20**. The dimers **11** and **20** were detritylated by exposure to $Cl_2CHCOOH$ and Et_3SiH in CH_2Cl_2 [3] to provide 68% of the alcohols **13** and **22**, respectively. Desilylation of the U*[s]U(*) dimers **9**, **11**, and **13**, and of the A*[s]A(*) dimers **18**, **20**, and **22** with $(HF)_3 \cdot Et_3N$ in THF [4] gave 58–87% of the isopropylidene protected mono- and dihydroxy compounds **10**, **12**, and **14**, and **19**, **21**, and **23**, respectively.

The formation of thioethers is evidenced by the typical upfield shift for C(5′/I) and CH_2–C(6/II) of **9**–**14** (*Table 4* in the *Exper. Part*) and **18**–**23** (*Table 6* in the *Exper. Part*). A lower degree of flexibility for the CH_2SCH_2 unit of the U*[s]U(*) dimers is suggested by larger $\Delta\delta$ values for the geminal C(5′/I)H_2 and CH_2–C(6 or 8/II) of the U*[s]U(*) dimers **9**–**14** than for the A*[s]A(*) dimers **18**–**23** (0.06–0.51 *vs.* $\leq$0.07 and 0.08–0.44 *vs.* $<$0.06 ppm; *Tables 3* and *5* in the *Exper. Part)*.

2. *Homoassociation of the U*[s]U(*) and A*[s]A(*) Dimers.* The homoassociation of the U*[s]U(*) and A*[s]A(*) dimers was investigated by ^{1}H-NMR spectroscopy. We first analysed the association on the basis of the concentration dependence of the

Scheme



a) MeONa, MeOH; 79% of **9**; 73% of **11**; 79% of **18**; 84% of **20**. *b*) $(HF)_3 \cdot Et_3N$, THF; 87% of **10**; 77% of **12**; 58% of **14**; 80% of **19**; 75% of **21**; 66% of **23**. *c*) Cl_2CHCO_2H, Et_3SiH, CH_2Cl_2; 68% of **13**; 68% of **22**. TDS = Thexyl(dimethyl)silyl (thexyl = 1,1,2-trimethylpropyl), MMTr = (monomethoxy)-trityl = (4-methoxyphenyl)diphenylmethyl.

chemical shift for H–N(3) of the U*[s]U(*) and for H_2N–C(6) of the A*[s]A(*) dimers ('shift concentration curves' (SCCs); compare [1]), and then determined the conformation of the dimers, particularly the orientation of the nucleobase and of the

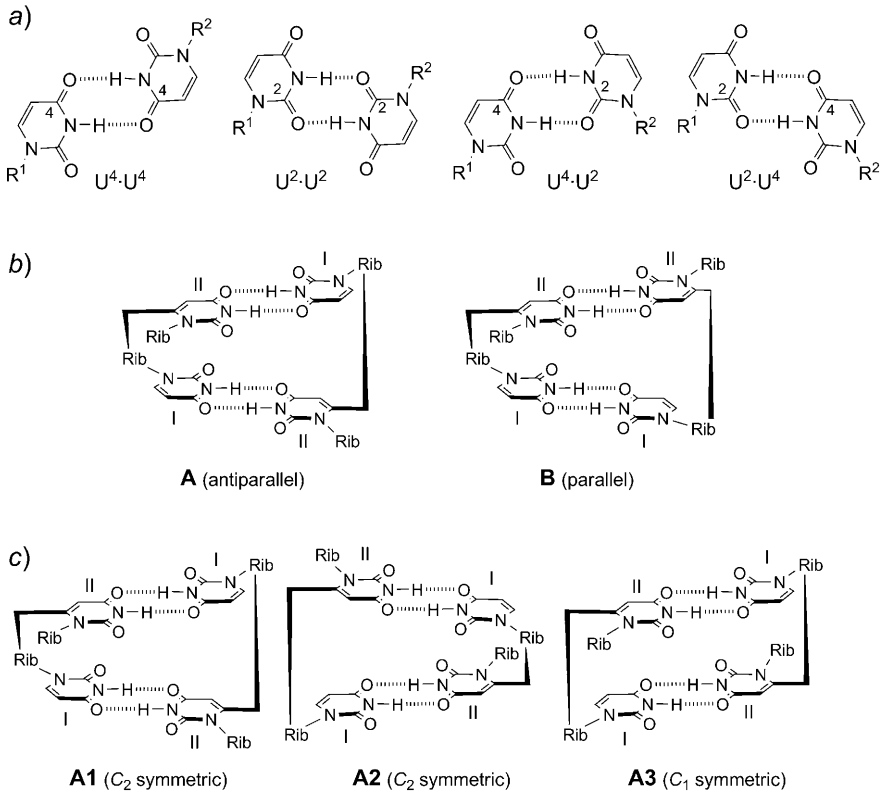


Fig. 2. a) *Homoassociation of 1-protected uracils* (R^1, $R^2 \neq H$). The superscripts in $U^x \cdot U^x$ indicate the C=O group involved in base pairing. b) *Antiparallel and parallel base pairing of cyclic duplexes derived from UU dimers* (illustrated for $U^4 \cdot U^4$ base pairing). c) *The three diastereoisomeric cyclic duplexes obtained from a given base-pairing mode* (illustrated for $U^4 \cdot U^4$ base pairing).

CH_2SCH_2 unit, at a concentration of 20–30 mM in $CHCl_3$, *i.e.,* at a concentration where substantial association is observed.

2.1. *Homoassociation of U*[s]U(*) Dimers. Ab initio* and semiempirical calculations suggest that *N(1)*-protected uracils pair in the gas phase, with C(4)=O and C(2)=O possessing similar H-accepting properties [5]. Hence, one expects the formation of a *ca.* 1:1:1:1 mixture of $U^4 \cdot U^4$, $U^2 \cdot U^2$, $U^4 \cdot U^2$, and $U^2 \cdot U^4$ duplexes (*Fig. 2,a*; the superscripts indicate the position of the H-accepting C=O group)[3]). If, in the duplexes shown in *Fig. 2,a*, $R^1 = R^2$, then $U^4 \cdot U^2$ and $U^2 \cdot U^4$ are identical, and a 1:1:2 mixture is expected, and a 1:1:1.6 mixture of $U^4 \cdot U^4$, $U^2 \cdot U^2$, and $U^4 \cdot U^2/U^2 \cdot U^4$ was indeed observed for a cold (123 K) solution of a uridine monomer in freon [6][7].

U*[s]U(*) Dimers may form a number of cyclic duplexes. The dimers may associate in an antiparallel fashion, as in **A**, or in a parallel one, as in **B** (*Fig. 2,b*). Any

[3]) $U^4 \cdot U^4$ and $U^2 \cdot U^2$ show the same relation of H-bonding as *Watson–Crick* and reverse *Watson–Crick* base pairing.

combination of $U^4 \cdot U^4$, $U^2 \cdot U^2$, $U^4 \cdot U^2$, and $U^2 \cdot U^4$ pairing of the two base units of the U*[s]U(*) monoplex must be taken into consideration. A given pairing mode allows the formation of four diastereoisomeric duplexes, best specified by the relative orientation of the ribosyl moieties of units II that are not an inherent part of the duplex, as illustrated in *Fig. 2,c*, for the duplex **A** possessing two $U^4 \cdot U^4$ base pairs. Two diastereoisomers possess ribosyl units on the same side of the base pairs (**A1** and **A2** in *Fig. 2,c*) and two on opposite sides (**A3**), meaning that two C_2-symmetric diastereoisomers (*i.e.*, **A1** and **A2**) and one C_1-symmetric diastereoisomer (*i.e.*, **A3**) of duplex **A** are feasible.

Some of the cyclic duplexes derived from U*[s]U(*) dimers may be disfavoured by steric interactions, *e.g.*, by an unfavourable orientation of the nucleobases, as it was observed in the U*[s]A(*) and A*[s]U(*) series [1], but the NMR spectra of U*[s]U(*) dimers in $CDCl_3$ should in any case reflect the equilibria between the monoplex, cyclic duplexes, and linear associates.

The U*[s]U(*) dimers **9**–**14** show different signals for H–N(3/I) and H–N(3/II). Unfortunately, broad NH signals in the HMBC spectrum of **14** prevent the observation of cross peaks between NH and C-atoms, and thus an unambiguous assignment of the NH signals. Deprotection of the silyloxy group at C(5′/II) of **11** to generate **12** went along with weak downfield shifts ($\leq$0.10 ppm for a *ca.* 20-mM solution) for both H–N(3), whereas deprotection of the $MMTrOCH_2$ group at C(2/I) of **11** was correlated with a strong downfield shift (*ca.* 1 ppm) for the more highly shielded H–N(3). Therefore, the more highly shielded NH signal of **11** and **12**, and the more highly deshielded one of **13** and **14** was tentatively assigned to H–N(3/I) (*Table 1*). H–N(3) of the *C(6/I)*-unsubstituted dimers **9** and **10** possess a similar chemical shift as the C(6/I)-substituted **11**, with the exception of H–N(3/I) of **9** resonating *ca.* 0.8 ppm downfield.

Table 1. *Chemical Shifts* [ppm] *of H–N(3) of the U*[s]U(*) Dimers* **9**–**14**, *and of* H_2N*–N(6) of the A*[s]A(*) Dimers* **18**–**23** *for 20–24-mM Solutions in* $CDCl_3$

	9	**10**	**11**	**12**	**13**	**14**
H–N(3/I)	10.78	10.02	9.96	10.02	10.97	11.08
H–N(3/II)	10.48	10.48	10.56	10.66	10.76	10.77
	18	**19**	**20**	**21**	**22**	**23**[a])
H_2N–N(6/I)	5.96	6.08	5.62	5.82	6.64	6.33
H_2N–N(6/II)	5.80	6.30	5.71	6.05	6.16	6.70

[a]) Assignments based on HMBC cross-peaks between H_2N–C(6/I) and C(5/I), between C(5/I) and H–C(2/I), between H–C(2/I) and C(4/I), and between C(4/I) and H–C(1′/I).

The concentration dependence of the chemical shift for both H–N(3) of **9**–**14** was determined for $CDCl_3$ solutions in the concentration range of 1 to 40–60 mM. The SCCs for **9**–**12** (*Fig. 3,a*) show the shape typical for an equilibrium between monoplex, linear and cyclic duplexes, and higher associates; *i.e.*, a low value for the chemical shift for H–N(3) at the lowest concentration where it can be measured, a weak bending of the SCC at concentrations below 20 mM, and a weak, continuous increase at higher concentrations. The SCCs of the uridine-6-methanol **13** are characterized by a strong

bending, typical for the formation of cyclic duplexes, but, instead of flattening out and forming a plateau, the chemical-shift values decrease slightly with increasing concentration (>19 mM; *Fig. 3,b*). This decrease is more pronounced for the SCCs of the corresponding diol **14** (decrease at a concentration >5 mM). The SCCs are moreover characterized by large shift values at the lowest concentration. We assume that the decrease is due to a shielding of the H–N(3) signals by stacking, as weakening of the H-bonds of the cyclic duplexes with increasing concentration is not easily envisaged. Stacking suggests that the cyclic duplexes (particularly of **14**) associate to higher aggregates. That the SCCs of **14** appear to again flatten out as the concentration is further increased above *ca.* 20 mM suggests a finite aggregation of the cyclic duplexes, probably due to intermolecular H-bonding of $HOCH_2$–C(6/I) (**13**), and of $HOCH_2$–C(6/I) and/or HO–C(5′/II) (**14**). At low concentrations, the mono-alcohol **13** exists mostly as the monoplex, and the diol **13** mostly in the form of one or several cyclic duplexes.

The SCCs in *Fig. 3* were analysed numerically by the method proposed by *Gutowsky* and *Saika* [8], including a value of 7.70 ppm for a 0.0001-mM solution [1][9][4]) (*Table 2*). For **13** and **14**, only the increasing δ values (up to maximum concentration of 19 and 5.2 mM, resp.) were used for the calculation. The ratio K_{ass} (H–N(3/II))/K_{ass} (H–N(3/I)) should be 1 for a cyclic duplex. It increases from 0.75 of **9** *via* 0.86 of **13** and 0.92 of **14** to 1.71 of **10** and **12**, and to 2.26 of **11**. In agreement with the above qualitative analysis, **13** and **14** show the strongest preference for the formation of cyclic duplexes. Values deviating from 1 evidence a higher proportion of linear associates, either involving a preferred association *via* U(II)*, as for **10**–**12**, or *via* U(I)(*), as for **9**. This is rationalized by the fact that 20% of **9** prefer an *anti*-orientation for unit I (see below), preventing the formation of cyclic duplexes, that base pairing for unit II in **10** and **12** is enhanced by co-operative H-bonding of HO–C(5′/II) and base pairing, and that the pairing properties for unit I of **11** and **12** are reduced due to the bulky MMTr group. As a consequence of the presence of higher associates, the calculated K_{ass} values are inaccurate, especially for **11**. Nevertheless, there is clear evidence for a correlation of base pairing and H-bonding of the OH groups, as seen by K_{ass} values increasing from 218–492 M^{-1} for the fully protected **9** and **11**, to 673–1405 M^{-1} for the monoalcohols **10**, **12**, and **13**, and to *ca.* 60000 for the diol **14**.

The ^{1}H-NMR spectra of 20–30-mM solutions of U*[s]U(*) dimers **9**–**14** in $CDCl_3$ (*Table 3* in the *Exper. Part*) suggest an equilibrium, mainly between linear and cyclic duplexes. The *syn*-conformation of unit II of the U*[s]U(*) dimers **9**–**14** is evidenced by the downfield shift of H–C(2′/II) resonating at 5.13–5.27 ppm. Similarly, the downfield shift of H–C(2′/I) (5.15–5.16 ppm) evidences the *syn*-conformation of unit I of the *C(6/I)*-substituted **11**, **12**, and **14**, whereas a slight upfield shift of 0.05–0.1 ppm for H–C(2′/I) of the *C(6/I)*-unsubstituted **9** and **10**, and of the *C(6/I)*-hydroxymethylated **13** suggests a *ca.* 4:1 *syn*/*anti* equilibrium. The *anti*-conformation of **13** may be favoured by an intramolecular H-bond to S–C(5′/I), as it was postulated for the corresponding A*[s]U* analogue [1]. Both ribosyl moieties of **9**–**14** show a strong

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[4]) This value corresponds to the value of monomeric uridines [1][6]. It leads to a lower variance of the K_{ass} values by partially correcting the error due to H/H exchange with residual H_2O in $CDCl_3$ at low concentrations [1].

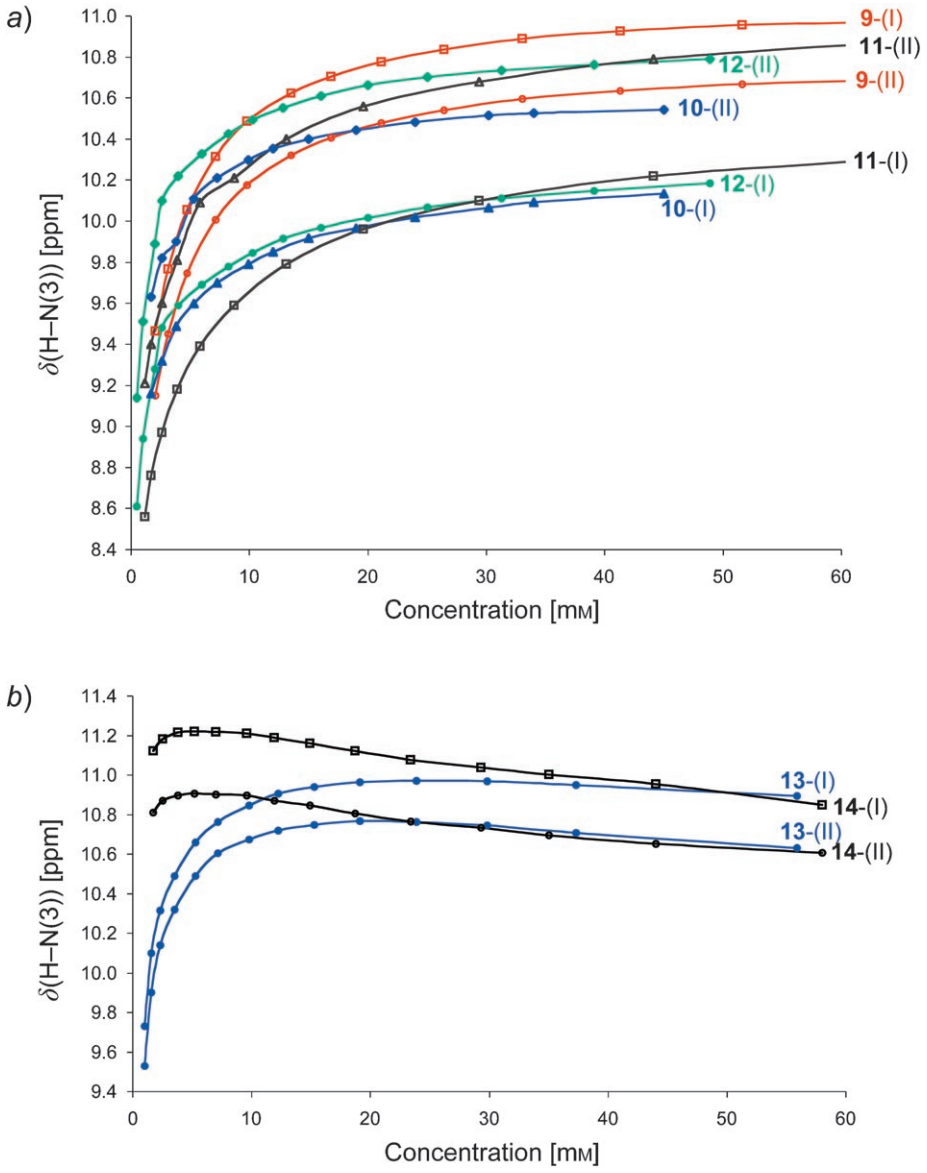

Fig. 3. *SCCs for H–N(3/I) and H–N(3/II) of the U*[s]U(*) dimers* **9**–**14** (1–60 mM) *in* $CDCl_3$ *solution* (including a value of 7.70 ppm for a 0.0001-mM soln.).

preference for the (*N*) conformation, as evidenced by $J(1',2')/J(3',4')$ of < 0.25. A *ca.* 4:1 *gt*/*tg* equilibrium for **9**–**14** is suggested by the observation that $J(4',5'a/I)$ is distinctly larger than $J(4',5'b/I)$ (8.7–9.6 *vs.* 1.0–4.8 Hz), assuming that the more highly deshielded H_a–C(5′/I) corresponds to $H_{pro\text{-}R}$, as it was established for dimers of the

Table 2. *Numerical Analysis*[a]) *of the SCCs of the U*[s]U(*) Dimers* **9**–**14** *in* Fig. 1: *Calculated* ^{1}*H-NMR Chemical Shifts* [ppm] *of H–N(3) of the Monoplex* ($c = 0$ mM) *and of the Cyclic Duplexes* ($c = \infty$), *and Calculated Association Constants* K_{ass} [M^{-1}].

	9	**10**	**11**	**12**	**13**[b])	**14**[b])
H–N(3/I)						
δ ($c = 0$ mM)	7.69 ± 0.11	7.70 ± 0.02	7.70 ± 0.03	7.69 ± 0.06	7.69 ± 0.10	7.65 ± 0.09
δ ($c = \infty$)	11.53 ± 0.09	10.46 ± 0.02	10.86 ± 0.03	10.48 ± 0.04	11.50 ± 0.09	11.37 ± 0.14
$\Delta\delta$ ($c = \infty$/30 mM)	0.66	0.40	0.76	0.38	0.53	
K_{ass}	441 ± 78	673 ± 31	218 ± 11	773 ± 93	1405 ± 260	64500 ± 95000
H–N(3/II)						
δ ($c = 0$ mM)	7.69 ± 0.12	7.70 ± 0.06	7.71 ± 0.08	7.69 ± 0.06	7.69 ± 0.13	7.66 ± 0.08
δ ($c = \infty$)	11.29 ± 0.09	10.88 ± 0.05	11.28 ± 0.07	11.09 ± 0.03	11.34 ± 0.13	11.05 ± 0.14
$\Delta\delta$ ($c = \infty$/30 mM)	0.71	0.37	0.60	0.37	0.59	
K_{ass}	329 ± 66	1150 ± 165	492 ± 63	1322 ± 127	1204 ± 306	59600 ± 88100

[a]) Including a value of 7.7 ppm for a 0.0001M soln. [b]) Only the increasing δ values at low concentration (**13**: up to $c = 19$ mM, **14**: up to $c = 5.2$ mM) are used for the numerical analysis. Due to only a few values and no value between 0.0001 and 1.7M, both K_{ass} values of **14** show a large variance although the curves fit well the experimental values.

A*[s]U(*) series [1]. According to this interpretation, the cyclic duplexes derived from the U*[s]U(*) dimers **9**–**14** prefer a *gt* conformation of unit I, similar as it was found for the cyclic duplexes derived from the self-complementary U*[s]A(*) dimers [1].

2.2. *Homoassociation of the A*[s]A(*) Dimers. Ab initio* and semiempirical calculations suggest that 9-substituted adenines pair in the gas phase, and that N(1) and N(7) show similar H-accepting properties [10]. One expects the formation of a *ca.* 1:1:1:1 mixture of $A^1 \cdot A^1$, $A^7 \cdot A^7$, $A^1 \cdot A^7$, and $A^7 \cdot A^1$ duplexes (*Fig. 4*; superscripts indicate the position of the H-accepting N-atom)[5]). For $R^1 = R^2$, $A^1 \cdot A^7$ and $A^7 \cdot A^1$ are identical. Steric interactions of a substituent at C(8) probably disfavour $A^1 \cdot A^7$, $A^7 \cdot A^1$, and especially $A^7 \cdot A^7$. As in the U*[s]U(*) series, A*[s]A(*) dimers may form a number of cyclic duplexes, and the four pairing modes, parallel *vs.* antiparallel pairing, and the fact that a given pairing mode may lead to three or four diastereoisomeric duplexes must be taken into consideration.

The A*[s]A(*) dimers **18**–**23** show broad ^{1}H-NMR signals for H_2N–C(6/I) and H_2N–C(6/II) (*Table 1*). HMBC Cross-peaks allowed an unambiguous assignment of the NH_2 signals of **23**, H_2N–C(6/I) resonating at higher fields than H_2N–C(6/II). Protection of both OH groups of **23** led to a strong upfield shift (0.71 and 0.99 ppm for a *ca.* 20-mM solution) for both NH_2 signals. The relative shielding observed upon protecting HO–C(5′/II) and $HOCH_2$–C(8/I) was used to tentatively assign the NH_2 signals of **18**–**22**.

A priori, one expects two signals of an NH_2 group involved in base pairing, with the H-donating NH resonating downfield with respect to the free NH. None of the NH_2 groups of **18**–**23** shows signal splitting, and the broad NH_2 signals evidence rapidly equilibrating H-atoms, and, thus, a weak and reversible association.

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[5]) $A^1 \cdot A^1$ and $A^7 \cdot A^7$ show the same relation of H-bonding as *Hoogsteen* and reverse-*Hoogsteen* base pairing.

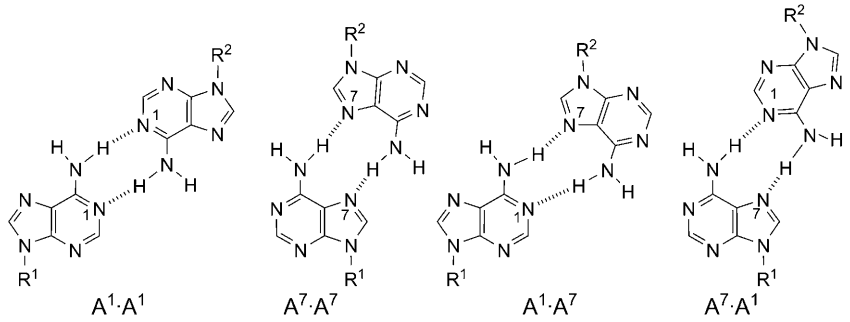

Fig. 4. *Homoassociation of 9-protected adenines* (R^1, $R^2 \neq H$). The superscripts in $A^x \cdot A^x$ indicate the H-accepting N-atom.

The concentration dependence of $\delta(NH_2)$ was measured for 1–60-mM solutions of **18**, **19**, and **21**–**23** in $CDCl_3$ (*Fig. 5*). The SCCs of **18**, **19**, and **21** show a nearly steady increase, evidencing equilibria of the monoplex with linear duplexes and higher associates. A slight flattening of the SCCs of **22** and **23** at concentrations above 20 mM hints at a minor participation also of cyclic duplexes. Since the broad NH_2 singlets evidence the equilibration of H-donating and free NH groups, a numerical analysis of the SCCs appears inappropriate.

The *syn*-conformation of unit II of the A*[s]A$^{(*)}$ silyl ethers **18**, **20**, and **22** is evidenced by the downfield shift of H–C(2′/II), resonating at 5.89–5.91 ppm (*Table 5* in the *Exper. Part*). An intramolecular H-bond from HO–C(5′/II) to N(3/II) of **18**, **20**, and **22** is evidenced by several characteristic parameters [1][2][11]; *i.e.*, by the downfield shift of HO–C(5′/II) (6.1–6.6 ppm), the upfield shift of H–C(2′/II) (5.19–5.24 ppm), small J(4′,5′a/II), J(4′,5′b/II), and J(5′a,OH/II) (< 1.5 Hz), a large J(5′b,OH/II) (10.5–11.5 Hz), and a (*S*) conformation (J(1′,2′)/J(3′,4′) > 4.4). Similarly as in the U*[s]A* series [1], H–C(2′/I) of the *C(8/I)*-unsubstituted **18** and **19** resonates upfield at 5.46 and 5.45 ppm, and H–C(2′/I) of the *C(8/I)*-substituted **20**–**23** at 5.53–5.65 ppm. This evidences a *ca.* 2:3 *syn*/*anti* equilibrium of **18** and **19**, and a *ca.* 2:1 *syn*/*anti* equilibrium of **20**–**23**. The *syn*-oriented adenine moiety of **18**–**23** and particularly the *anti*-oriented, *C(8/I)*-substituted adenine moiety of **20**–**23** disfavour the *gg*-orientation of the thiomethyl group, an expectation that agrees with J(4′,5′a/I) and J(4′,5′b/I) of 5.5–7.5 Hz, suggesting a *ca.* 1:1 equilibrium of *gt*- and *tg*-conformers of **18**–**23**. The ribosyl unit I of **18**–**23** and the ribosyl unit II of the silyl ethers **18**, **20**, and **22** prefer a (*N*) conformation, as evidenced by J(1′,2′)/J(3′,4′) of 0.4–0.65.

3. *Heteroassociation of the U*[s]U$^{(*)}$ and A*[s]A$^{(*)}$ Dimers.* In $CDCl_3$ and in $CDClF_2/CDF_3$ solution, 1-alkylated uracils and 9-alkylated adenines form U·A hetero-duplexes ($K_{ass} < 250$ M^{-1}) rather than U·U and A·A homo-duplexes [10–15]. 4,13-Bis(aden-9-ylpropyl)- and 4,13-bis(thymid-1-ylpropyl)-4,13-diaza-18-crown-6 compounds associate in $CDCl_3$ with $K_{ass} = 855$ M^{-1} [16]. This suggests that hetero-association should also be preferred for U*[s]U$^{(*)}$ and A*[s]A$^{(*)}$ dimers in $CDCl_3$ solution.

The hetero-duplexation was investigated with the completely protected U*[s]U* dimer **11** and A*[s]A* dimer **20**. The SSCs for H–N(3/I) and H–N(3/II) of **11** were

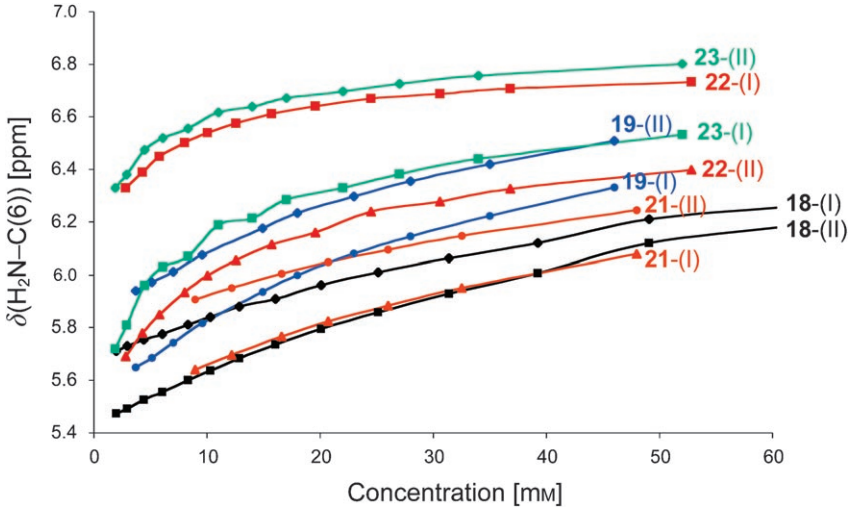

Fig. 5. *SCCs for $H_2N-C(6/I)$ and $H_2N-C(6/II)$ of the A*[s]A(*) dimers* **18**, **19**, *and* **21**–**23** (1–60 mM) *in $CDCl_3$ solution*

determined for $CDCl_3$ solutions of equimolar mixtures of **11** and **20**, and compared to the ones for solutions of **11** only (*Fig. 6,a*). The hetero-duplexation of the corresponding monoalcohols **13** and **22** was investigated in a similar way (*Fig. 6,b*). Hetero-pairing is clearly favoured over homo-pairing by these thiomethylene-linked U*[s]U* and A*[s]A* dimers, as evidenced by the strongly differing chemical shifts for H–N(3/I) and H–N(3/II) of **11** and **13** in the presence of **20** or **22**, respectively, at concentrations larger than 10 mM ($\Delta\delta \geq 1$ ppm). The chemical shifts of 11.7 to 12 ppm for H–N(3/I) and H–N(3/II) of the mixture **11**/**20** and **13**/**22** at concentrations of 30 mM suggest the formation of duplexes *via Hoogsteen* and *Watson–Crick* pairing[6]). The weaker bending of the SCCs for **11**/**20** at concentrations above 15 mM, as compared to the SCCs for **13**/**22**, evidences that the transformation of the linear to the cyclic duplex(es) is less favoured for the hetero-duplexes **11** · **20** than for **13** · **22**.

The slight upfield shift for H–N(3/I) and H–N(3/II) of **13** at higher concentrations that was rationalised by assuming association of the cyclic duplexes effects a downsizing of K_{ass} irrespective of weather it is obtained by numerical or graphical analysis, as the basic equations were not corrected by including higher associates. For this reason, the calculated K_{ass} values for the hetero-duplexation of **11** and **20** (289 ± 59 M^{-1} for H–N(3/I) and 455 ± 105 M^{-1} for H–N(3/II)) are too small as compared with K_{ass} for the homo-duplexation of **11** (218 ± 11 M^{-1} for H–N(3/I) and 492 ± 63 M^{-1} for H–N(3/II)). The K_{ass} values for the hetero-duplexation of **13** and **22** (1733 ± 174 M^{-1} for H–N(3/I) and 2025 ± 241 M^{-1} for H–N(3/II)) are more precise, being larger than

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[6]) Compare with 12.6–12.8 ppm for *Watson–Crick* base-paired U*[s]A(*) cyclic duplexes and 11.0 ppm for a reverse *Hoogsteen* base-paired A*[s]U* cyclic duplex [1].

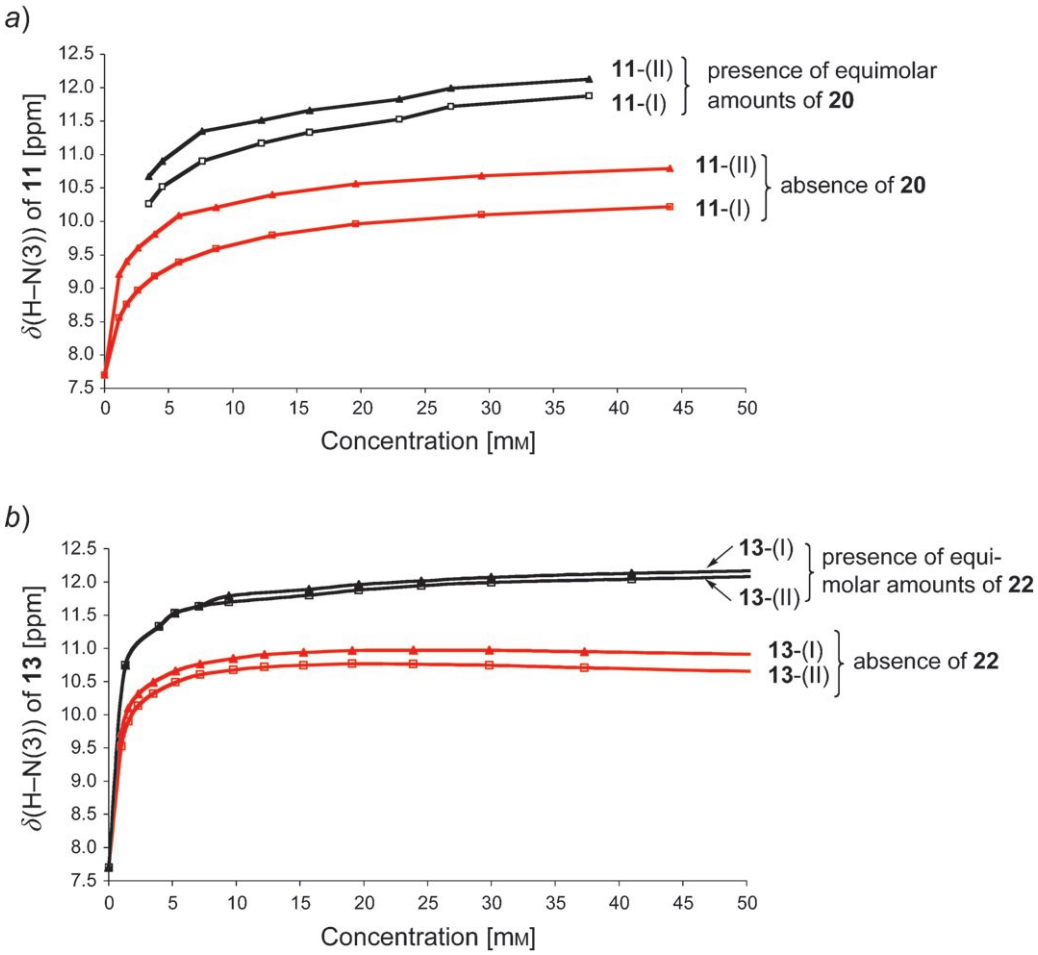

Fig. 6. *SCCs for H–N(3/I) and H–N(3/II) of the U*[s]U* dimers* **11** *and* **13** (1–50 mM) *in* $CDCl_3$ *solution in the presence or absence of equimolar amounts of the A*[s]A* dimers* **20** *and* **22**, *respectively* (the assignment of the H–N(3) signals in the presence of the A*[s]A* dimers is tentative)

the K_{ass} values for the homo-duplexation of **13** (1450 ± 260 M^{-1} for H–N(3/I) and 1204 ± 306 M^{-1} for H–N(3/II)).

The 1:1 stoichiometry of the hetero-duplexation of **11** and **20** was determined by a *Job*'s plot that was derived by analysing the chemical shifts of H–N(3/I) and H–N(3/II) of **11** (*Fig. 7* and *Exper. Part*) upon adding increasing amounts of **20**. For the calculation of the *Job*'s plot, the following δ values were used: 7.70 ppm for H–N(3/I) and H–N(3/II) of **11**, 12.81 ppm for H–N(3/I) of **11**·**20**, and 12.90 ppm for H–N(3/II) of **11**·**20**[7]). The determination of the *Job*'s plot is not trivial, as excess **11** in the 6:4

[7]) The latter two values correspond to the δ(HN) values at infinite concentration as obtained in the numerical analysis of the SCCs of **11**/**20** in *Fig. 6,a*.

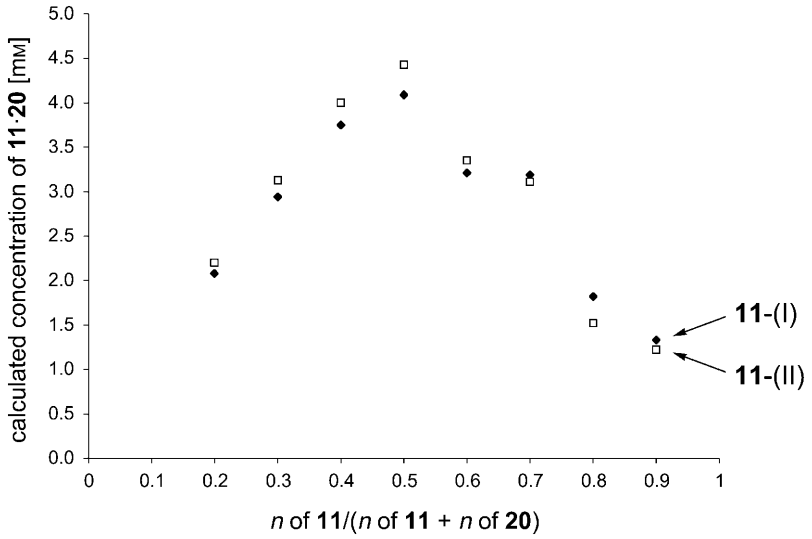

Fig. 7. Job*'s plot revealing the 1:1 hetero-association of the U*[s]U* dimer* **11** *and the A*[s]A** dimer* **20**

to 9:1 **11**/**20** mixtures forms homo-duplexes, and $\delta = 7.70$ ppm for the monoplex **11** cannot be used in the calculation. The above mixtures were, therefore, considered as consisting of a 1:1 mixture of **11** and **20**, and excess **11** forming the homoduplex **11** · **11**, and $\delta = 7.70$ ppm was replaced by the δ(H–N(3/I)) and δ(H–N(3/II)) values for **11** (at the concentration resulting from the 6:4 to 9:1 ratio of **11** and **20**), as taken from the SSCs in *Fig. 3* (values given in the *Exper. Part*). The resulting *Job*'s plot confirms the 1:1 stoichiometry of the hetero-duplexation, although the correction of the δ(H–N) values for **11** is only an approximation, as indicated by the dissymmetry of the plot.

The determination of the stoichiometry of duplexation by the mole-ratio method does not require knowledge of the chemical shift values of the monoplexes and duplexes. We analyzed the chemical shift of both H–N(3) for solutions of the U*[s]U$^{(*)}$ dimers maintaining the concentration of the U*[s]U$^{(*)}$ dimer constant and varying the concentration of the A*[s]A$^{(*)}$ dimer (*Fig. 8* and *Exper. Part*). The pairs **9**/**18** and **12**/**21** show different curves for H–N(3/I) and H–N(3/II), whereas the curves for H–N(3/I) and H–N(3/II) of **10**/**19** and **14**/**23** overlap partially, and those of **13**/**22** completely. A 1:1 association is evidenced by a crossing of the lines indicating the gradients a low and at high mole ratios at a mole ratio of 1. This condition is fulfilled more or less well for H–N(3/I) of **9**/**18** and **10**/**19**, and for H–N(3/II) of **14**/**23**. The stronger deviation for H–N(3/II) of **9**/**18**, and for H–N(3) of both **12**/**21** and **13**/**22** may evidence larger amounts of higher linear associates.

The calculation of the K_{ass} values for the heteropairing of U*[s]U$^{(*)}$ and A*[s]A$^{(*)}$ dimers from mole-ratio experiments requires reliable data for the homopairing of the U*[s]U$^{(*)}$ dimers. Since the data in *Table 2* show a large variance, further calculations appeared inappropriate. Nevertheless, K_{ass} for the U*[s]U$^{(*)}$/A*[s]A$^{(*)}$ heteropairing appears to be *ca.* 1.5–2 times larger than K_{ass} for the U*[s]U$^{(*)}$/U*[s]U$^{(*)}$ homopairing, as suggested by the dilution experiment for **13**/**22**.

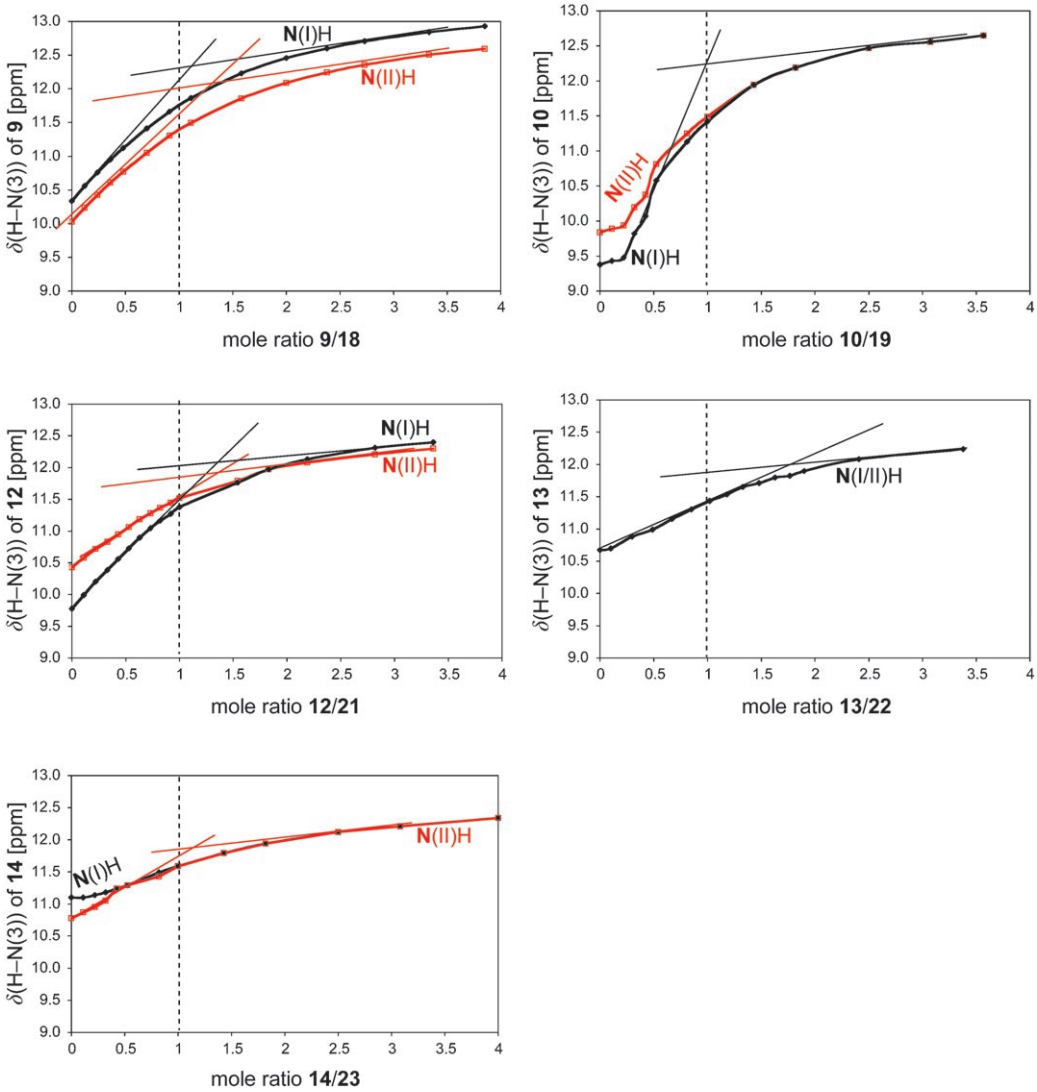

Fig. 8. *Mole-ratio plots for the chemical shifts of H–N(3/I) and H–N(3/II) of the U*[s]U′(*) dimers* **9**, **10**, *and* **12**–**14** *involved in hetero-association to the corresponding A*[s]A′(*) dimers* **18**, **19**, *and* **21**–**23**, *respectively*

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

Experimental Part

General. See [1].

5′-O-*[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′*-O-*isopropylideneuridine-6-methyl-(6¹ → 5′*-S)-*2′,3′*-O-*isopropylidene-5′-thiouridine* (**9**). A soln. of **6** [1] (328 mg, 0.8 mmol) and **7** [1] (205 mg, 0.8 mmol) in

O_2-free MeOH (2 ml) was treated with a soln. of MeONa (43 mg, 1 mmol) in O_2-free MeOH (2 ml), stirred for 14 h at r.t., and evaporated. A soln. of the residue in CH_2Cl_2 was washed with NH_4Cl soln. and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/cyclohexane 3:2 → 4:1) gave **9** (484 mg, 79%). Colourless foam. R_f (MeOH/CH_2Cl_2 5:95) 0.28. M.p. 128.3–130.6°. $[\alpha]_D^{25} = -11.5$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3387*w*, 3170*w*, 2961*m*, 2929*m*, 2868*w*, 1715*s*, 1696*s*, 1609*w*, 1455*m*, 1380*m*, 1271*w*, 1236*m*, 1157*m*, 1072*s*, 981*w*, 876*m*, 838*m*. ^{1}H-NMR (300 MHz, 50 mM, $CDCl_3$): see *Table 3*; additionally, 10.95, 10.70 (2 br. *s*, 2 NH); 1.58 (*sept.*, $J = 6.9$, Me_2CH); 1.52, 1.30 (2*s*, 2 Me_2CO_2); 0.83 (*d*, $J = 6.9$, Me_2CH); 0.81 (*s*, Me_2CSi); 0.08, 0.06 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 114.10, 113.55 (2*s*, 2 Me_2CO_2); 34.08 (*d*, Me_2CH); 27.35, 27.09, 25.39, 25.31 (4*q*, 2 Me_2CO_2); 25.22 (*s*, Me_2CSi); 20.42 (*q*, Me_2CSi); 18.58 (*q*, Me_2CH); −3.07 (*q*, Me_2Si). HR-MALDI-MS: 761.2866 ($[M+Na]^+$, $C_{33}H_{50}N_4NaO_{11}SSi^+$; calc. 761.2864). Anal. calc. for $C_{33}H_{50}N_4O_{11}SSi$ (738.92): C 53.64, H 6.82, N 7.58; found: C 53.86, H 7.05, N 7.29.

2′,3′-O-*Isopropylidene-6-methyluridine-(6¹ → 5′*-S*)-2′,3′*-O-*isopropylidene-5′-thiouridine* (**10**). In a polyethylene flask, a soln. of **9** (40 mg, 0.05 mmol) and $(HF)_3 \cdot Et_3N$ (80 µl) in THF (1 ml) [4] was stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/MeOH 100:0 → 92:8) gave **10** (28 mg, 87%). Colourless foam. R_f (AcOEt/MeOH 9:1) 0.50. $[\alpha]_D^{25} = -46.2$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3478*w* (br.), 3387*w*, 3028*w*, 2994*m*, 2928*m*, 1697*s*, 1621*w*, 1454*m*, 1383*m*, 1266*w*, 1157*w*, 1086*m*, 1069*m*, 908*w*, 879*m*, 861*m*. ^{1}H-NMR (300 MHz, 50 mM, $CDCl_3$): see *Table 3*; additionally, 10.57, 10.15 (2 br. *s*, 2 NH); 1.54, 1.33 (2*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 114.32, 113.97 (2*s*, 2 Me_2C); 27.42, 27.14, 25.38, 25.27 (4*q*, 2 Me_2C). HR-MALDI-MS: 619.1689 ($[M+Na]^+$, $C_{25}H_{32}N_4NaO_{11}S^+$; calc. 619.1686).

5′-O-*[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′*-O-*isopropylideneuridine-6-methyl-(6¹ → 5′*-S*)-2′,3′*-O-*isopropylidene-6-{[(4-methoxyphenyl)diphenylmethoxy]methyl}-5′-thiouridine* (**11**). A soln. of **6** (592 mg, 0.918 mmol) and **8** [1] (490 mg, 0.918 mmol) in O_2-free MeOH (2 ml) was treated with a soln. of MeONa (194 mg, 3.6 mmol) in O_2-free MeOH (2 ml), stirred for 14 h at r.t., and evaporated. A soln. of the residue in CH_2Cl_2 was washed with sat. NH_4Cl soln. and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/cyclohexane 3:2 → 4:1) gave **11** (688 mg, 73%). Colourless foam. R_f (MeOH/CH_2Cl_2 5:95) 0.43. $[\alpha]_D^{25} = -36.9$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3387*w*, 3171*w* (br.), 2961*m*, 2868*w*, 1697*s* (br.), 1609*w*, 1510*w*, 1448*m*, 1383*m*, 1302*w*, 1269*w*, 1157*w*, 1069*m*, 981*w*, 876*w*, 837*m*. ^{1}H-NMR (300 MHz, 65 mM, $CDCl_3$): see *Table 3*; additionally, 10.88, 10.34 (2 br. *s*, 2 NH); 7.48–7.25 (*m*, 12 arom. H); 6.85 (*d*, $J = 8.7$, 2 arom. H); 3.80 (*s*, MeO); 1.58 (*sept.*, $J = 6.9$, Me_2CH); 1.53, 1.43, 1.33, 1.28 (4*s*, 2 Me_2CO_2); 0.83 (*d*, $J = 6.9$, Me_2CH); 0.80 (*s*, Me_2CSi); 0.05, 0.04 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 158.85, 143.09, 142.96, 133.96 (4*s*); 130.26 (2*d*); 128.10 (4*d*); 127.99 (4*d*); 127.32 (2*d*); 113.85 (*s*, 2 Me_2CO_2); 113.34 (2*d*); 88.31 (*s*, Ph_3C); 55.27 (*q*, MeO); 34.13 (*d*, Me_2CH); 27.31, 27.22, 25.44, 25.35 (4*q*, 2 Me_2CO_2); 25.35 (*s*, Me_2CSi); 20.43, 20.38 (2*q*, Me_2CSi); 18.54 (*q*, Me_2CH); −3.19 (*q*, Me_2Si). HR-MALDI-MS: 1063.4155 ($[M+Na]^+$, $C_{52}H_{68}N_4NaO_{13}SSi^+$; calc. 1063.4171).

2′,3′-O-*Isopropylideneuridine-6-methyl-(6¹ → 5′*-S*)-2′,3′*-O-*isopropylidene-6-{[(4-methoxyphenyl)diphenylmethoxy]methyl}-5′-thiouridine* (**12**). In a polyethylene flask, a soln. of **11** (100 mg, 0.096 mmol) in THF (1.5 ml) was treated with $(HF)_3 \cdot Et_3N$ (156 µl, 0.96 mmol), stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/cyclohexane 4:1) gave **12** (60 mg, 77%). Colourless crystals. R_f (MeOH/CH_2Cl_2 5:95) 0.23. $[\alpha]_D^{25} = -59.8$ ($c = 1.0$, $CHCl_3$). M.p. 151.0–152.9°. IR ($CHCl_3$): 3386*w* (br.), 3182*w*, 3019*w*, 2929*w*, 1707*s* (br.), 1610*w*, 1510w, 1449*m*, 1384*m*, 1222*m*, 1157*w*, 1086*m*, 1035*w*, 875*w*, 837*m*, 790*m*, 728*m*. ^{1}H-NMR (300 MHz, 6 mM, $CDCl_3$): see *Table 3*; additionally, 10.75, 10.15 (2 br. *s*, 2 NH); 7.48–7.25 (*m*, 12 arom. H); 6.85 (*d*, $J = 8.7$, 2 arom. H); 3.80 (*s*, MeO); 1.53, 1.42, 1.33, 1.28 (4*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 159.22, 143.44, 143.31, 134.29 (4*s*); 130.59 (2*d*); 128.42 (4*d*); 128.34 (4*d*); 127.66 (2*d*); 114.15 (*s*, 2 Me_2C); 113.63 (2*d*); 88.45 (*s*, (4-$MeOC_6H_4$)Ph_2C); 55.47 (*q*, MeO); 27.48, 27.30, 25.65, 25.46 (2*q*, 2 Me_2C). HR-MALDI-MS: 921.2997 ($[M+Na]^+$, $C_{46}H_{50}N_4NaO_{13}S^+$; calc. 921.2993). Anal. calc. for $C_{46}H_{50}N_4O_{13}S$ (898.31): C 61.46, H 5.61, N 6.23; found: C 61.38, H 5.86, N 6.04.

5′-O-*[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′*-O-*isopropylideneuridine-6-methyl-(6¹ → 5′*-S*)-2′,3′*-O-*isopropylidene-6-(hydroxymethyl)-5′-thiouridine* (**13**). A soln. of **11** (100 mg, 0.09 mmol) in CH_2Cl_2

Table 3. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the U*[s]U$^{(*)}$ Dimers* **9**–**14** *in $CDCl_3$*

	9 (50 mM)	**10** (50 mM)	**11** (65 mM)	**12** (6 mM)	**13** (40 mM)	**14** (60 mM)[a])
Uridine unit I						
H–C(5/I)	5.68	5.74	5.69[b])	5.665[b])	5.86[b])	5.93
H–C(6/I)	7.36	7.23	–	–	–	–
CH_a–C(6/I)	–	–	4.04	4.03	4.60–4.43	4.58
CH_b–C(6/I)	–	–	3.97	3.97	4.60–4.43	4.48
$HOCH_2$–C(6/I)	–	–	–	–	4.19[c])	3.95–3.90
H–C(1′/I)	5.785	5.68	5.65	5.665	5.78[b])	5.675
H–C(2′/I)	5.06	5.11	5.15	5.16	5.08	5.15
H–C(3′/I)	4.74	4.84	4.87–4.80	4.84	4.76	4.85
H–C(4′/I)	4.34	4.31	4.18–4.09	4.21–4.12	4.375	4.33
H_a–C(5′/I)	3.12	3.04	2.97	3.01	3.23	3.14
H_b–C(5′/I)	2.73	2.83	2.83	2.81	2.72	2.78
J(5,6/I)	8.1	8.1	–	–	–	–
J(H_a,H_b/I)	–	–	12.6	12.6	[d])	13.8
J(1′,2′/I)	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0
J(2′,3′/I)	6.3	6.3	6.6	6.6	6.3	6.3
J(3′,4′/I)	4.8	4.2	[d])	4.8	5.1	5.1
J(4′,5′a/I)	9.0	8.7	8.7	9.0	9.6	9.6
J(4′,5′b/I)	3.6	4.2	4.8	4.5	3.0	< 1.5
J(5′a,5′b/I)	14.4	14.4	14.4	14.4	14.4	14.1
Uridine unit II						
H–C(5/II)	5.37	5.42	5.665[b])	5.65[b])	5.81[b])	5.72
CH_a–C(6/II)	3.88	3.73	3.59	3.62	3.93	3.88–3.80
CH_b–C(6/II)	3.48	3.55	3.51	3.49	3.49	3.54
H–C(1′/II)	5.835	5.80	5.775	5.73	5.82[b])	5.84
H–C(2′/II)	5.16	5.23	5.27	5.25	5.15	5.135
H–C(3′/II)	4.83	4.95	4.87–4.80	4.97	4.865	4.91
H–C(4′/II)	4.09	4.19	4.18–4.09	4.21–4.12	4.12	4.20
H_a–C(5′/II)	3.78	3.88–3.76	3.77	3.82–3.72	3.90–3.78	3.88–3.80
H_b–C(5′/II)	3.78	3.88–3.76	3.72	3.82–3.72	3.90–3.78	3.88–3.80
HO–C(5′/II)	–	3.38–3.22	–	3.19–3.08	–	4.90–4.75
J(H_a,H_b/II)	15.9	15.3	15.0	15.0	15.6	15.0
J(1′,2′/II)	< 1.0	< 1.0	1.5	1.8	< 1.0	< 1.0
J(2′,3′/II)	6.3	6.3	6.3	6.6	6.3	6.3
J(3′,4′/II)	3.9	4.8	[d])	4.2	4.2	4.8
J(4′,5′a/II)	6.3	3.9	5.1	[d])	4.8	[d])
J(4′,5′b/II)	6.3	3.9	7.2	[d])	7.2	[d])
J(5′a,5′b/II)	[d])	[d])	10.8	[d])	[d])	[d])

[a]) Assignments based on DQFCOSY, HSQC, and HMBC spectra. [b]) Assignments may be interchanged. [c]) Broad *t*, *J* = 7.2 Hz. [d]) Not assigned.

(1 ml) was treated with $Cl_2CHCOOH$ (100 µl, 1.21 mmol) and Et_3SiH (122 µl, 0.76 mmol) [3], stirred for 15 min at r.t., poured into sat. $NaHCO_3$ soln., and extracted with AcOEt. The combined org. layers were washed with brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/cyclohexane 4:1 → 1:0) gave **13** (50 mg, 68%). Colourless crystals. R_f (MeOH/CH_2Cl_2 5:95) 0.28. $[\alpha]_D^{25} = -21.3$ ($c = 1.0$, $CHCl_3$). M.p. 125.4–126.7°. IR ($CHCl_3$): 3388*w* (br.), 3184*w* (br.), 3027*w*, 2961*m*, 2930*m*, 2869*w*, 1706*s* (br.), 1697*s*, 1621*w*, 1457*m*, 1383*m*, 1265*w*, 1158*m*, 1086*m*, 1069*m*, 875*w*, 837*m*. ^{1}H-NMR (300 MHz, 40 mM,

Table 4. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the U*[s]U$^{(*)}$ Dimers* **9**–**14** *in $CDCl_3$*

	9	**10**	**11**	**12**	**13**	**14**[a])
Uridine unit I						
C(2/I)	149.85	150.00	150.68	151.16	150.92	150.89
C(4/I)	164.52	164.04	163.67	163.98	164.46	164.52
C(5/I)	102.39	102.71	103.31	103.64	101.60	100.94
C(6/I)	144.44	143.77	151.95	152.18	155.37	155.76
CH_2–C(6/I)	–	–	62.38	62.65	60.86	60.23
C(1′/I)	97.12	97.07	91.95[b])	92.38[b])	91.81[b])	91.31
C(2′/I)	84.37	84.26[c])	84.30[c])	84.41[c])	84.85[c])	84.62
C(3′/I)	84.37	83.94[c])	84.61[c])	84.88[c])	85.07[c])	84.80
C(4′/I)	90.79[b])	90.25[b])	89.97[b])	90.50[b])	91.81[b])	91.68
C(5′/I)	34.08	33.25	32.95	33.42	33.13	33.05
Uridine unit II						
C(2/II)	150.48	151.24	151.77	151.70	151.38	151.48
C(4/II)	163.53	162.53	163.25	162.99	163.95	163.38
C(5/II)	103.29	104.06	103.91	104.37	103.57	104.09
C(6/II)	151.83	151.66	151.95	152.18	152.47	152.21
CH_2–C(6/II)	32.62	33.06	32.95	33.32	32.84	32.96
C(1′/II)	90.95[b])	91.49[b])	91.41[b])	91.85[b])	91.41[b])	91.41
C(2′/II)	84.37	84.02[c])	84.11[c])	84.07[c])	84.67[c])	84.34
C(3′/II)	81.79	80.51	82.20	80.76	82.10	80.43
C(4′/II)	89.72[b])	88.29	89.81[b])	88.58	90.29[b])	88.35
C(5′/II)	64.25	62.82	64.04	62.96	64.58	62.57

[a]) Assignments based on HSQC and HMBC spectra. [b]) [c]) Assignments may be interchanged.

$CDCl_3$): see *Table 3*; additionally, 10.75, 10.15 (2 br. *s*, 2 NH); 1.61 (*sept.*, *J* = 6.9, Me_2CH); 1.53, 1.31 (2*s*, 2 Me_2CO_2); 0.86 (*d*, *J* = 6.9, *Me*$_2$CH); 0.84 (*s*, Me_2CSi); 0.125, 0.11 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 114.11, 113.98 (2*s*, Me_2CO_2); 34.24 (*d*, Me_2CH); 27.55, 27.30, 25.60, 25.36 (4*q*, 2 *Me*$_2$CO$_2$); 25.36 (*s*, Me_2CSi); 20.58, 20.53 (2*q*, *Me*$_2$CSi); 18.73, 18.68 (2*q*, *Me*$_2$CH); −2.97 (*q*, Me_2Si). HR-MALDI-MS: 791.2971 ($[M+Na]^+$, $C_{34}H_{52}N_4NaO_{12}SSi^+$; calc. 791.2969). Anal. calc. for $C_{34}H_{52}N_4O_{12}SSi$ (768.31): C 53.11, H 6.82, N 7.29; found: C 53.22, H 6.80, N 7.09.

*2′,3′-*O*-Isopropylideneuridine-6-methyl-(6^1 → 5′-*S*)-2′,3′-*O*-isopropylidene-6-(hydroxymethyl)-5′-thiouridine* (**14**). In a polyethylene flask, a soln. of **13** (105 mg, 0.136 mmol) in THF (1 ml) was treated with $(HF)_3 \cdot Et_3N$ (220 µl, 1.36 mmol), stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/MeOH 100 : 0 → 92 : 8) gave **14** (52 mg, 58%). Colourless foam. R_f (MeOH/CH_2Cl_2 8 : 92) 0.42. $[\alpha]_D^{25} = -35.1$ (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3387*w* (br.), 3182*w*, 3028*w*, 3013*w*, 2929*m*, 2857*w*, 1698*s* (br.), 1621*w*, 1457*w*, 1384*m*, 1268*w*, 1158*m*, 1099*m*, 1065*m*, 985*w*, 908*w*, 875*w*, 748*m*. ^{1}H-NMR (500 MHz, 60 mM, $CDCl_3$, assignments based on DQFCOSY, HSQC, and HMBC spectra): see *Table 3*; additionally, 10.84, 10.56 (2 br. *s*, 2 NH); 1.54, 1.32 (2*s*, Me_2C/II); 1.52 1.31 (2*s*, Me_2C/I). ^{13}C-NMR (125 MHz, $CDCl_3$, assignments based on a HSQC and a HMBC spectrum): see *Table 4*; additionally, 114.27 (*s*, Me_2C/II); 113.99 (*s*, Me_2C/I); 27.35, 25.35 (2*q*, *Me*$_2$C/II); 27.09, 25.16 (2*q*, *Me*$_2$C/I). HR-MALDI-MS: 649.1794 ($[M+Na]^+$, $C_{26}H_{34}N_4NaO_{12}S^+$; calc. 649.1792).

*5′-*O*-[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′-*O*-isopropylideneadenosine-8-methyl-(8^1 → 5′-*S*)-2′3′-*O*-isopropylidene-5′-thioadenosine* (**18**). Under N_2, a soln. of **15** [1] (297 g, 0.49 mmol) and **16** [1] (232 mg, 0.49 mmol) in O_2-free MeOH (1 ml) was treated dropwise with a soln. of MeONa (280 mg, 5.1 mmol) in O_2-free MeOH (1 ml), stirred for 12 h at r.t., and evaporated. A soln. of the residue in AcOEt was washed with NH_4Cl soln. and brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/

NH_4OH 100:0:0 → 90:10:1) gave **18** (307 mg, 79%). Yellowish powder. R_f (CH_2Cl_2/MeOH/NH_4OH 90:10:1) 0.50. $[\alpha]_D^{25} = -55.2$ ($c = 1.0$, $CHCl_3$). M.p. 116.1–118.8°. IR ($CHCl_3$): 3413*w*, 2981*w*, 2961*s*, 2862*m*, 1632*s*, 1589*m*, 1472*w*, 1423*w*, 1375*m*, 1329*w*, 1294*w*, 1249*m*, 1087*s*, 869*m*. ^{1}H-NMR (300 MHz, 22 mM, $CDCl_3$): see *Table 5*; additionally, 5.99 (br. *s*, NH_2); 5.84 (br. *s*, NH_2); 1.53 (*sept.*, $J = 6.9$, Me_2CH); 1.60, 1.59, 1.40, 1.36 (4*s*, 2 Me_2CO_2); 0.81 (*d*, $J = 6.9$, Me_2CH); 0.76, 0.75 (2*s*, Me_2CSi); −0.055, −0.07 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 114.31, 113.60 (2*s*, 2 Me_2CO_2); 34.07 (*d*, Me_2CH); 27.22, 27.08, 25.47, 25.36 (4*q*, 2 Me_2CO_2); 25.21 (*s*, Me_2CSi); 20.31 (*q*, Me_2CSi); 18.49 (*q*, Me_2CH); −3.40 (*q*, Me_2Si). HR-MALDI-MS: 807.3412 (99, $[M+Na]^+$, $C_{35}H_{52}N_{10}NaO_7SSi^+$; calc. 807.3408), 785.3585 (100, $[M+H]^+$, $C_{35}H_{53}N_{10}O_7SSi^+$; calc. 785.3589). Anal. calc. for $C_{35}H_{52}N_{10}O_7SSi$ (784.35): C 53.55, H 6.68, N 17.84; found.: C 53.48, H 6.81, N 17.82.

*2′,3′-*O*-Isopropylideneadenosine-8-methyl-(8^I → 5′-*S*)-2′3′-*O*-isopropylidene-5′-thioadenosine* (**19**). In a polyethylene flask, a soln. of **18** (40 mg, 0.05 mmol) in THF (1 ml) was treated with $(HF)_3 \cdot Et_3N$ (80 µl), stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/NH_4OH 100:0:0 → 100:10:1) gave **19** (26 mg, 80%). Colourless foam. R_f (CH_2Cl_2/MeOH/NH_4OH 90:10:1) 0.30. $[\alpha]_D^{25} = -65.0$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3524*w*, 3483*w*, 3412*m*, 3331*w* (br.), 3260*w*, 3199*w* (br.), 2993*m*, 2943w, 1635*s*, 1589*m*, 1473*w*, 1455*w*, 1424w, 1375*m*, 1331*w*, 1297*w*, 1266*m*, 1155*w*, 1082*s*, 1010*w*, 909*w*, 863*w*. ^{1}H-NMR (300 MHz, 40 mM, $CDCl_3$): see *Table 5*; additionally, 6.46 (br. *s*, NH_2); 6.27 (br. *s*, NH_2); 1.63, 1.58, 1.365, 1.35 (4*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 114.71, 114.15 (2*s*, 2 Me_2C); 27.99, 27.24, 25.60, 25.51 (4*q*, 2 Me_2C). HR-MALDI-MS: 665.2232 ($[M+Na]^+$, $C_{27}H_{34}N_{10}NaO_7S^+$; calc. 665.2230).

*5′-*O*-[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′-*O*-isopropylideneadenosine-8-methyl-(8^I → 5′-*S*)-2′3′-*O*-isopropylidene-8-{[(4-methoxyphenyl)diphenylmethoxy]methyl}-5′-thioadenosine* (**20**). A soln. of **15** (1 g, 1.3 mmol) and **17** [1] (779 mg, 1.3 mmol) in O_2-free MeOH (1 ml) was treated dropwise with a soln. of MeONa (280 mg, 5.1 mmol) in O_2-free MeOH (1 ml), stirred for 12 h at r.t., and evaporated. A soln. of the residue in AcOEt was washed with NH_4Cl soln. and brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/NH_4OH 95:5:1) gave **20** (1.18 g, 84%). Yellowish foam. R_f (CH_2Cl_2/MeOH/NH_4OH 95:5:1) 0.26. $[\alpha]_D^{25} = -47.2$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3412*w*, 2982*s*, 2865*m*, 1686*s*, 1634*s*, 1602*m*, 1585*m*, 1510*m*, 1448*m*, 1376*m*, 1300*m*, 1253*s*, 1081*s*, 866*m*. ^{1}H-NMR (300 MHz, 20 mM, $CDCl_3$): see *Table 5*; additionally, 7.54–7.48 (*m*, 4 arom. H); 7.42–7.22 (*m*, 8 arom. H); 6.85 (*d*, $J = 8.7$, 2 arom. H); 5.71 (br. *s*, NH_2); 5.62 (br. *s*, NH_2); 3.79 (*s*, MeO); 1.52 (*sept.*, $J = 6.9$, Me_2CH); 1.59, 1.50, 1.39, 1.36 (4*s*, 2 Me_2CO_2); 0.80 (*d*, $J = 6.9$, Me_2CH); 0.75, 0.74 (2*s*, Me_2CSi); −0.07, −0.09 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 158.67 (*s*); 143.33 (2*s*); 134.40 (*s*); 130.39 (2*d*); 128.34 (4*d*); 127.93 (4*d*); 127.13 (2*d*); 114.05, 113.55 (2*s*, 2 Me_2CO_2); 113.26 (2*d*); 87.89 (*s*, (4-$MeOC_6H_4$)Ph_2C); 55.26 (*q*, MeO); 34.10 (*d*, Me_2CH); 27.21 (2 C), 25.57, 25.48 (3*q*, 2 Me_2CO_2); 25.24 (*s*, Me_2CSi); 20.33 (*q*, Me_2CSi); 18.52 (*q*, Me_2CH); −3.41 (*q*, Me_2Si). HR-MALDI-MS: 1109.4698 ($[M+Na]^+$, $C_{56}H_{70}N_{10}NaO_9SSi^+$; calc. 1109.4715).

*2′,3′-*O*-Isopropylideneadenosine-8-methyl-(8^I → 5′-*S*)-2′3′-*O*-isopropylidene-8-{[(4-methoxyphenyl)-diphenylmethoxy]methyl}-5′-thioadenosine* (**21**). In a polyethylene flask, a soln. of **20** (100 mg, 0.07 mmol) and $(HF)_3 \cdot Et_3N$ (150 µl, 0.93 mmol) in THF (2 ml) was stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/NH_4OH 100:0:0 → 92:9:1) gave **21** (65 mg, 75%). Colourless foam. R_f (CH_2Cl_2/MeOH/NH_4OH 95:5:1) 0.13. $[\alpha]_D^{25} = -46.7$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3523*w*, 3450*w*, 3411*w*, 3170*w*, 3020*s*, 2990*m*, 1687*s*, 1635*s*, 1602*m*, 1510*m*, 1448*m*, 1376*m*, 1331*w*, 1299*m*, 1224*s*, 1155*m*, 1081*s*, 866*m*, 789*m*, 728*s*. ^{1}H-NMR (300 MHz, 24 mM, $CDCl_3$): see *Table 5*; additionally, 7.52–7.48 (*m*, 4 arom. H); 7.41–7.24 (*m*, 8 arom. H); 6.85 (*d*, $J = 8.7$, 2 arom. H); 6.06 (br. *s*, NH_2); 5.85 (br. *s*, NH_2); 3.78 (*s*, MeO); 1.60, 1.49, 1.35, 1.34 (4*s*, 2 Me_2C). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 158.74 (*s*); 143.24 (2*s*); 134.27 (*s*); 130.39 (2*d*); 128.32 (4*d*); 127.96 (4*d*); 127.21 (2*d*); 114.29, 113.96 (2*s*, 2 Me_2C); 113.33 (2*d*); 87.99 (*s*, (4-$MeOC_6H_4$)Ph_2C); 55.32 (*q*, MeO); 27.81, 27.21, 25.59, 25.50 (4*q*, 2 Me_2C). HR-MALDI-MS: 967.3542 ($[M+Na]^+$, $C_{48}H_{52}N_{10}NaO_9S^+$; calc. 967.3537).

*5′-*O*-[Dimethyl(1,1,2-trimethylpropyl)silyl]-2′,3′-*O*-isopropylideneadenosine-8-methyl-(8^I → S-5′)-8-(hydroxymethyl)-2′3′-*O*-isopropylidene-5′-thioadenosine* (**22**). A soln. of **20** (300 mg, 0.27 mmol) in CH_2Cl_2 (3 ml) was treated with $CH_2CHCOOH$ (300 µl, 3.6 mmol) and Et_3SiH (300 µl, 1.88 mmol),

Table 5. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the A*[s]A$^{(*)}$ Dimers* **18**–**23** *in $CDCl_3$*

	18 (22 mM)	**19** (40 mM)	**20** (20 mM)	**21** (24 mM)	**22** (15 mM)	**23** (52 mM)[a])
Adenosine unit I						
H–C(2/I)	8.32[b])	8.325[b])	8.29[b])	8.27[b])	8.26[b])	8.18
H–C(8/I)	8.08	7.99	–	–	–	–
CH_a–C(8/I)	–	–	4.43	4.41	5.01	4.94
CH_b–C(8/I)	–	–	4.43	4.41	5.01	4.91
*H*OCH_2–C(8/I)	–	–	–	–	2.0–1.75	2.4–2.1
H–C(1′/I)	6.12	6.10	6.18[c])	6.17	6.16	6.295
H–C(2′/I)	5.45	5.46	5.65	5.645	5.53	5.63
H–C(3′/I)	5.09	5.005	5.06	5.10	5.08	5.12
H–C(4′/I)	4.24	4.47	4.22	4.31	4.23	4.415
H_a–C(5′/I)	2.88	2.925	2.835	2.935	2.76	2.865
H_b–C(5′/I)	2.88	2.925	2.835	2.865	2.76	2.83
J(H_a,H_b/I)	–	–	[d])	[d])	[d])	15.1
J(1′,2′/I)	1.8	1.8	1.8	1.8	1.5	1.7
J(2′,3′/I)	6.3	6.3	6.3	6.6	6.6	6.4
J(3′,4′/I)	3.0	3.3	2.7	3.3	3.0	3.6
J(4′,5′a/I)	6.6	6.6	6.9	7.5	6.6	7.2
J(4′,5′b/I)	6.6	6.6	6.9	6.3	6.6	5.5
J(5′a,5′b/I)	[d])	[d])	[d])	14.1	[d])	14.2
Adenosine unit II						
H–C(2/II)	8.26[b])	8.24[b])	8.24[b])	8.21[b])	8.22[b])	8.155
CH_a–C(8/II)	3.92	3.90	3.875	3.84	4.08	3.89
CH_b–C(8/II)	3.92	3.825	3.82	3.74	3.81	3.793
H–C(1′/II)	6.20	5.99	6.20[c])	5.94	6.39	5.98
H–C(2′/II)	5.89	5.24	5.89	5.195	5.91	5.23
H–C(3′/II)	5.00	5.08	5.08	5.04	5.04	5.05
H–C(4′/II)	4.46	4.50	4.30	4.45	4.445	4.49
H_a–C(5′/II)	3.615	3.945	3.59	3.90	3.57	3.93
H_b–C(5′/II)	3.505	3.80	3.475	3.73	3.475	3.778
HO–C(5′/II)	–	6.09	–	6.60	–	6.62–6.45
J(H_a,H_b/II)	[d])	15.0	15.0	15.0	14.7	15.0
J(1′,2′/II)	1.8	5.1	1.8	5.1	1.5	4.9
J(2′,3′/II)	6.3	6.3	6.3	6.0	6.3	5.8
J(3′,4′/II)	3.3	< 1.0	3.3	0.9	3.9	1.1
J(4′,5′a/II)	6.6	< 1.0	6.9	< 1.0	6.9	< 0.5
J(4′,5′b/II)	6.3	< 1.0	6.3	< 1.0	6.3	< 0.5
J(5′a,5′b/II)	10.8	12.6	10.8	12.9	10.5	11.4
J(5′a,OH/II)	–	< 1.5	–	< 1.5	–	< 1.5
J(5′b,OH/II)	–	10.5	–	11.1	–	11.3

[a]) Assignments based on DQFCOSY, HSQC, and HMBC spectra. [b]) [c]) Assignments may be interchanged. [d]) Not assigned.

stirred for 15 min, poured into sat. $NaHCO_3$ soln., and extracted with AcOEt. The combined org. layers were washed with brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/NH_4OH 100:0:0 → 90:10:1) gave **22** (150 mg, 68%). Colourless powder. R_f (CH_2Cl_2/MeOH/NH_4OH 90:10:1) 0.31. $[\alpha]_D^{25} = -44.7$ ($c = 1.0$, $CHCl_3$). M.p. 128.1–129.3°. IR ($CHCl_3$): 3521*w*, 3480*w*, 3412*w*, 3327*w* (br.), 3180*w*

Table 6. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the A*[s]A$^{(*)}$ Dimers* **18**–**23** *in $CDCl_3$*

	18	**19**	**20**	**21**	**22**	**23**[a])
Adenosine unit I						
C(2/I)	152.93	153.41	152.74	150.26[b])	152.88	152.90
C(4/I)	150.31	150.03	150.45	149.62[c])	150.27	150.15
C(5/I)	120.03	120.34	118.84[b])	118.65[d])	117.97	118.01
C(6/I)	155.26[b])	155.79[b])	155.12[c])	153.64[e])	155.17[b])	155.27
C(8/I)	139.93	140.27	149.04	149.82	151.27	151.45
CH_2–C(8/I)	–	–	59.34	59.15	57.42	57.41
C(1′/I)	89.91	90.85	89.92	89.88	89.34	89.55
C(2′/I)	83.76	83.99	83.87	84.00	83.81	83.63
C(3′/I)	84.10	84.42	84.19	84.00	84.17	84.15
C(4′/I)	87.81	87.69	87.82	87.99	88.34	88.55
C(5′/I)	33.36	34.01	33.36	33.72	32.96	33.43
Adenosine unit II						
C(2/II)	152.42	152.50	152.28	149.94[b])	152.44	152.26
C(4/II)	148.80	149.22	150.23	149.39[c])	150.16	149.62
C(5/II)	118.40	119.17	118.45[b])	118.48[d])	117.97	118.48
C(6/II)	155.85[b])	155.98[b])	154.76[c])	154.15[e])	154.98[b])	155.42
C(8/II)	148.58	148.34	148.89	148.95	149.00	148.41
CH_2–C(8/II)	28.10	28.57	28.11	28.43	27.78	28.03
C(1′/II)	90.60	92.27	89.92	91.86	89.98	91.94
C(2′/II)	82.87	82.85	82.88	82.75	82.78	82.63
C(3′/II)	82.04	81.87	82.08	81.53	82.11	81.60
C(4′/II)	86.97	85.95	87.14	85.72	87.93	85.83
C(5′/II)	62.80	63.52	62.82	63.13	62.78	63.19

[a]) Assignments based on HSQC and HMBC spectra. [b]) [c]) [d]) [e]) Assignments may be interchanged.

(br.), 2961*m*, 2867*w*, 1636*s*, 1593*m*, 1474*w*, 1442*w*, 1375*m*, 1330*m*, 1295*m*, 1257*m*, 1089*s*, 972*w*, 930*w*, 866*m*. ^{1}H-NMR (300 MHz, 15 mM, $CDCl_3$): see *Table 5*; additionally, 6.57 (br. *s*, NH_2); 6.11 (br. *s*, NH_2); 1.52 (*sept.*, *J* = 6.9, Me_2CH); 1.60, 1.59, 1.395, 1.375 (4*s*, 2 Me_2CO_2); 0.79 (*d*, *J* = 6.9, Me_2CH); 0.74, 0.73 (2*s*, Me_2CSi); −0.08, −0.09 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 114.74, 113.62 (2*s*, 2 Me_2CO_2); 34.09 (*d*, Me_2CH); 27.22, 27.13, 25.48, 25.43 (2*q*, 2 Me_2CO_2); 25.22 (*s*, Me_2CSi); 20.32 (*q*, Me_2CSi); 18.49 (*q*, Me_2CH); −3.40 (*q*, Me_2Si). HR-MALDI-MS: 837.3516 (100, $[M+Na]^+$, $C_{36}H_{54}N_{10}NaO_8SSi^+$; calc. 837.3514), 815.3682 (39, $[M+H]^+$, $C_{36}H_{55}N_{10}O_8SSi^+$; calc. 815.3694). Anal. calc. for $C_{36}H_{54}N_{10}O_8SSi$ (814.36): C 53.05, H 6.68, N 17.19; found: C 53.19, H 6.80, N 17.18.

2′,3′-O-*Isopropylideneadenosine-8-methyl-(8^I → 5′*-S*)-8-(hydroxymethyl)-2′3′*-O-*isopropylidene-5′-thioadenosine* (**23**). In a polyethylene flask, a soln. of **22** (60 mg, 0.07 mmol) and $(HF)_3 \cdot Et_3N$ (120 µl, 0.75 mmol) in THF (1 ml) was stirred for 2 d at r.t., poured into brine, and extracted with AcOEt. The combined org. layers were washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH/NH_4OH 100:0:0 → 92:8:1) gave **23** (33 mg, 66%). Colourless powder. R_f (CH_2Cl_2/MeOH/NH_4OH 90:10:1) 0.14. M.p. 149.1–150.8°. UV ($CHCl_3$): 263 (24768). $[\alpha]_D^{25} = -39.3$ (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): 3481*w*, 3411*w*, 3332*w* (br.), 3265*w*, 3187*w* (br.), 2993*m*, 2841*w*, 1638*s*, 1600*m*, 1480*w*, 1448*w*, 1375*m*, 1332*m*, 1297*m*, 1157*m*, 1082*s*, 1008*w*, 968*w*, 909*w*, 864*w*. ^{1}H-NMR (500 MHz, 52 mM, $CDCl_3$; assignments based on DQFOSY, HSQC, and HMBC spectra): see *Table 5*; additionally, 6.80 (br. *s*, H_2N–C(6/II)); 6.54 (br. *s*, H_2N–C(6/I)); 1.62, 1.35 (2*s*, Me_2C/II); 1.57, 1.37 (2*s*, Me_2C/I). ^{13}C-NMR (125 MHz, $CDCl_3$, assignments based on a HSQC and a HMBC spectrum): see *Table 6*; additionally, 114.53 (*s*, Me_2C/I); 113.95 (*s*, Me_2C/II); 27.73, 25.38 (2*q*, Me_2C/II); 27.06, 25.36 (2*q*, Me_2C/I). HR-MALDI-MS: 695.2324 ($[M+Na]^+$, $C_{28}H_{36}N_{10}NaO_8S^+$; calc. 695.2336).

Job*'s Plot for the Heteroduplexation of* **11** *and* **20** (*Fig. 7*). 20-mM Solns. of **11** and **20** were mixed in varying proportions in such a way that the sum of the concentrations of **11** and **20** was 20 mM, and the chemical shifts of H–N(3/I) and H–N(3/II) were determined. For the calculation, we used the δ values of 7.70 ppm for H–N(3/I) and H–N(3/II) of **11**, 12.81 ppm for H–N(3/I) of **11**·**20**, and 12.90 ppm for H–N(3/II) of **11**·**20**. 6:4 to 9:1 Mixtures of **11** and **20** were considered as composed of a 1:1 mixture of **11/20** and excess **11**. For these mixtures, δ(H–N(3/I)) and δ(H–N(3/II)) of **11**, as taken from the curves in *Fig. 6*, were 9.8 and 10.4 ppm for 9:1 and 8:2 $[c]_0$ ratios, 9.5 and 10.2 ppm for the 7:3 $[c]_0$ ratio, and 9.2 and 9.8 ppm for the 6:4 $[c]_0$ ratio, respectively. ^{1}H-NMR (300 MHz, $CDCl_3$): 10.17 (H–N(3/I)) and 10.77 (H–N(3/II)) for 9:1 $[c]_0$ ratio of **11/20**; 10.37 and 10.88 for 8:2 $[c]_0$ ratio; 10.76 and 11.20 for 7:3 $[c]_0$ ratio; 10.81 and 11.24 for 6:4 $[c]_0$ ratio; 11.18 and 11.54 for 5:5 $[c]_0$ ratio; 11.69 and 12.03 for 4:6 $[c]_0$ ratio; 11.87 and 12.22 for 3:7 $[c]_0$ ratio; 12.14 and 12.48 for 2:8 $[c]_0$ ratio.

Mole-Ratio Plots for the Heteroduplexation of **9/18**, **10/19**, **12/21**, **13/22**, *and* **14/23** (*Fig. 8*). In a NMR tube, 0.8 or 0.9 ml of a 6M soln. of **9**, 2.8M soln. of **10**, 6.3M soln. of **12**, 6M soln. of **13**, and 3.2M soln. of **14** were diluted repeatedly with aliquots of a soln. containing the U*[s]U$^{(*)}$ dimer in the same concentration and the corresponding A*[s]A$^{(*)}$ dimer in the tenfold concentration, respectively. The chemical shifts for H–N(3/I) and H–N(3/II) of the U*[s]U$^{(*)}$ dimers were determined and plotted against the U*[s]U$^{(*)}$/A*[s]A$^{(*)}$ mole ratio.

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