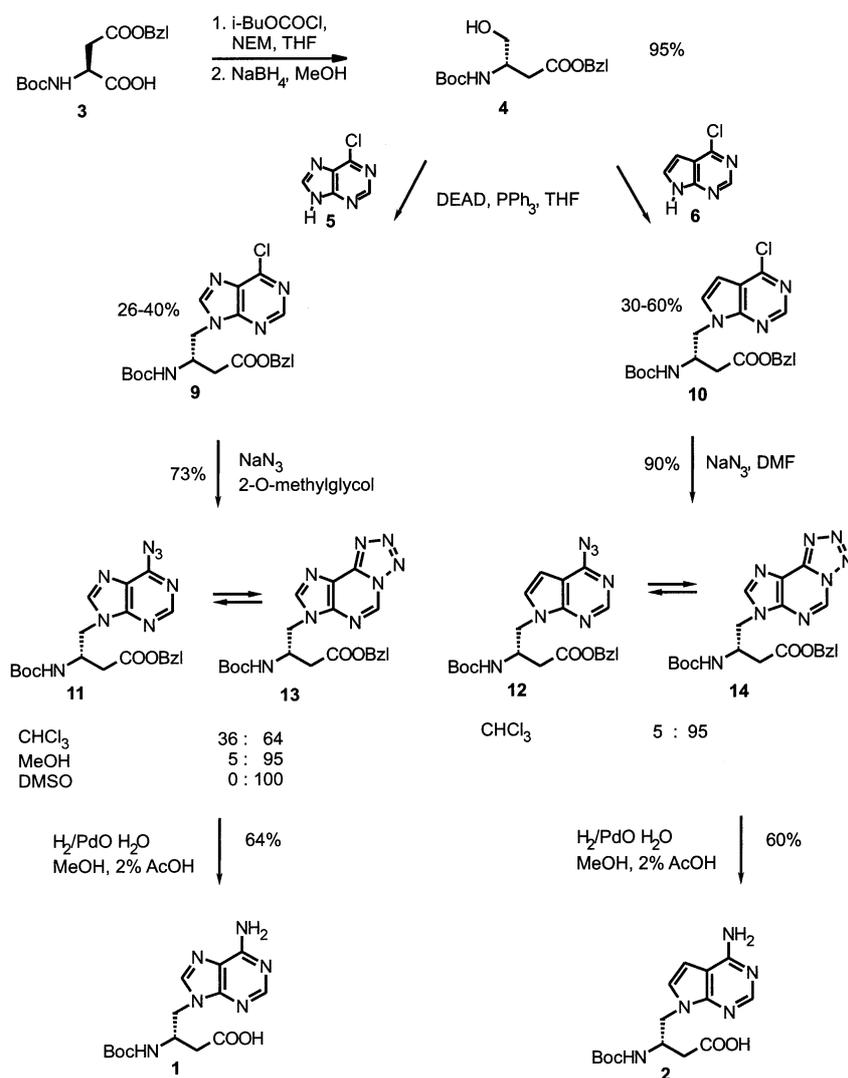


key step for the synthesis of nucleo- β -amino acids is the substitution of a purine or pyrimidine at the γ -position of the β -homoserine using the Mitsunobu reaction^[8]. The required β -homoserine derivative **4** was available by reduction of the C-terminal carbonyl group of Boc-L-Asp(Bzl)-OH (**3**) in 95% yield^[9]. 6-Chloropurine (**5**) and 6-chloro-7-carbapurine (**6**) were used because adenine failed in the Mitsunobu reaction. 6-Chloro-7-carbapurine (**6**) was synthesized by the Davoll procedure starting with bromacetaldehyde diethyl acetal (**7**) and ethyl cyanoacetate (**8**) in four steps (Scheme 3)^[10].

amino acid **9** were obtained, so the Mitsunobu reaction leading to the 7-carba analogon **10** was performed at -78°C adding DEAD to a mixture of β -homoserine (**4**), 6-chloro-7-carbapurine (**6**), and triphenylphosphane in THF. The conversion of *N*-Boc-amino acids into *N*-Boc-aziridines under Mitsunobu conditions appears to predominate as the competing reaction^[11]. Therefore, the Mitsunobu reagents and 6-chloro-7-carbapurine (**6**) were dissolved in THF at -78°C and added to a solution of β -homoserine derivative *ent*-**4** in THF at -20°C in a latter experiment. The yield was improved to 60%, probably due to suppres-

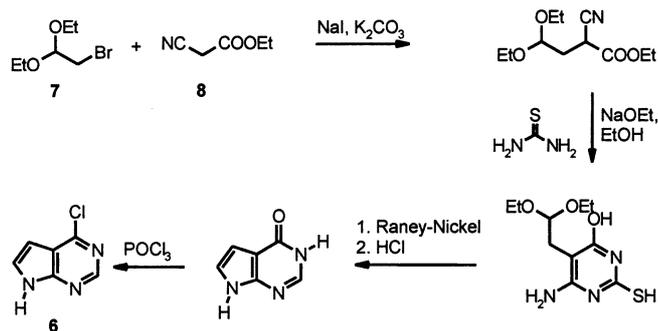
Scheme 2. Synthesis of the nucleo amino acids Boc-adeninyl- β -homoserine (**1**) and Boc-7-carbaadeninyl- β -homoserine (**2**) using the Mitsunobu reaction as the key step for connecting the nucleobases with the side chain of the β -amino acid



The Mitsunobu reaction is known to be useful, e.g. for connecting nucleobases to propanoic acid derivatives^[8a], to the anomeric position of furanoses^[8g] and to carbocycles^[8c]^[8d]. The reaction conditions vary with regard to temperature (reflux or -78°C) and to the sequence for adding the components. By analogy to these procedures, the β -homoserine derivative **4** was added to 6-chloropurine (**5**) together with DEAD and triphenylphosphane in THF at room temperature. Only modest yields (26–40%) of nucleo

amino acids **9** or **10** were obtained, so the Mitsunobu reaction leading to the 7-carba analogon **10** was performed at -78°C adding DEAD to a mixture of β -homoserine (**4**), 6-chloro-7-carbapurine (**6**), and triphenylphosphane in THF. The conversion of *N*-Boc-amino acids into *N*-Boc-aziridines under Mitsunobu conditions appears to predominate as the competing reaction^[11]. Therefore, the Mitsunobu reagents and 6-chloro-7-carbapurine (**6**) were dissolved in THF at -78°C and added to a solution of β -homoserine derivative *ent*-**4** in THF at -20°C in a latter experiment. The yield was improved to 60%, probably due to suppres-

Scheme 3. Synthesis of 6-chloro-7-carbapurine (**6**) following a procedure of Davoll^[10]



led to transesterification with 2-*O*-methylglycol. As known from the literature the azidopurines **11** and **12** are in a solvent-dependent equilibrium with the tetrazole derivatives **13** and **14**, respectively^[14]. In chloroform, the tetrazole isomer **13** is favored by 2:1 compared to the azidopurine **11**, whereas the equilibrium of tetrazole **14** and 6-azido-7-carbapurine **12** is 19:1, as determined by ¹H-NMR spectroscopy. In methanol or DMSO the tetrazole isomer **13** predominates.

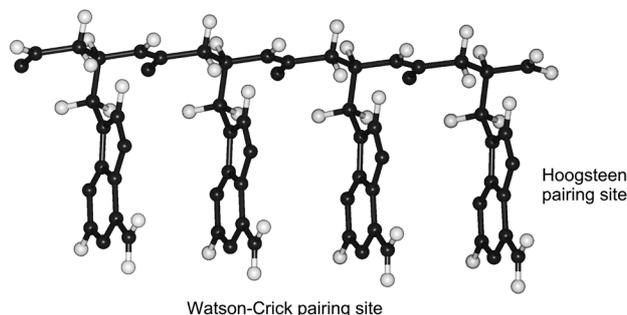
The nucleic amino acids **1** and **2** were oligomerized by solid-phase peptide synthesis (SPPS) on a 4-methylbenzhydrylamine-(MBHA)-polystyrene support loaded with (*R*)-lysine(*Z*)-OH (*Z* = benzylloxycarbonyl)^[15]. A fourfold excess of nucleic amino acid was coupled in DMF using *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) and *N,N*-diisopropylethylamine for activation. Each coupling step was performed with at least 97% yield. Purification of the oligomers by HPLC (RP-C18) was followed by characterization using electrospray-ionisation mass spectrometry (ESI-MS) and ¹H-NMR spectroscopy (see Experimental Section).

Adenine–Adenine Pairing of β -PNA Oligomers

Simple model studies of a β -homoalanyl-PNA single strand show particular potential for the formation of higher ordered structures (Scheme 4). In the extended backbone conformation, a homochiral β -homoalanyl-PNA strand provides a uniform orientation of all side chains. Therefore, all adenine bases are uniformly aligned and all Watson-Crick and Hoogsteen pairing sites each have the same order of donor/acceptor functionalities and the same orientation. As a consequence, purinyl- β -homoalanyl-PNA in the extended conformation provides two pairing planes based on all Watson–Crick sites and on all Hoogsteen sites, respectively.

The adenine–adenine self-pairing is not observed in B-DNA^[16] because of the helix topology but is known for oligomers with nearly linear backbones^[17]. We examined A–A pairing in the β -PNA series by synthesis of the three sequences H-(β -HalA)₆-Lys-NH₂ (**15**), H-(β -HalA)₅-Lys-NH₂ (**16**), and H-(β -HalA)₄-Lys-NH₂ (**17**) which differ only in length [β -HalA = γ -(adenine-9-yl)- β -(*S*)-homoalanine, Lys-NH₂ = (*R*)-lysine amide^[15]]^[6]. The stabilities of hexa-

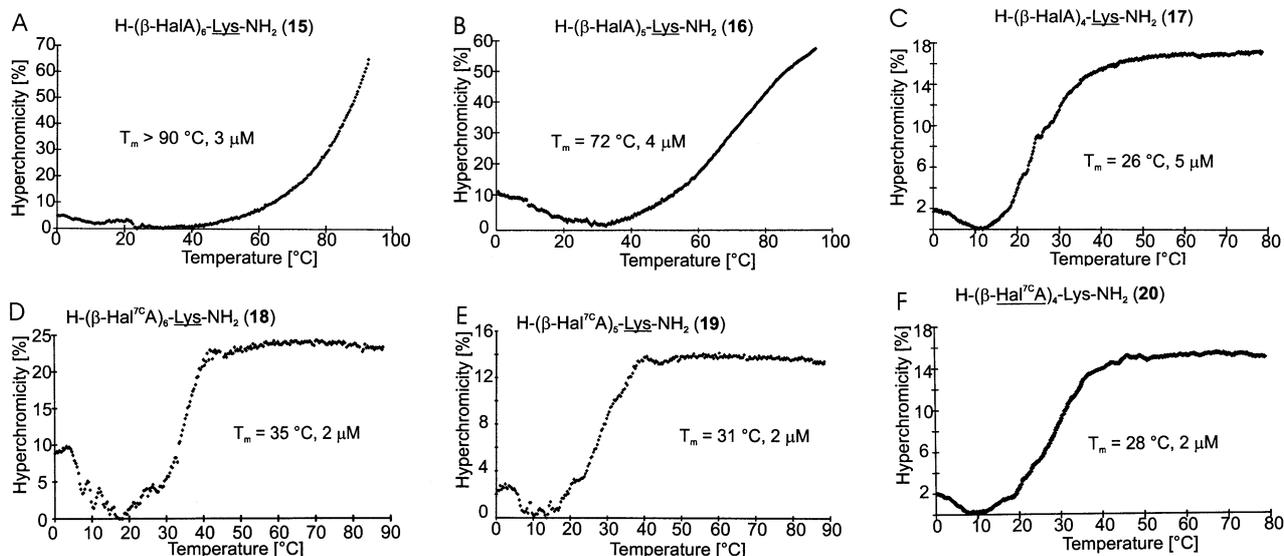
Scheme 4. β -Homoalanyl-PNA in the extended backbone conformation provides uniform alignment of all nucleobases; all Watson–Crick sites, as well as all Hoogsteen sites simultaneously spread pairing planes suitable for recognition which could lead to higher ordered structures



mer **15** ($T_m > 90^\circ\text{C}$, $> 70\%$ hyperchromicity, $3 \mu\text{M}$) and pentamer **16** ($T_m = 72^\circ\text{C}$, $> 60\%$ hyperchromicity, $4 \mu\text{M}$) were extraordinarily high (Schemes 5A and 5B). Even tetramer **17** formed a reasonably stable double strand ($T_m = 26^\circ\text{C}$, 16% hyperchromicity, $5 \mu\text{M}$) (Scheme 5C). The stabilities (T_m) and hyperchromicities were determined by UV melting curves. As destacking of the nucleobases results in an increase of UV absorption, cooperative dissociation of a double strand can be recognized as a sigmoidal-shaped curve when measuring absorption with increasing temperature. Therefore, the melting curves mainly result from nucleobase interactions. UV and CD measurements were performed in an aqueous solution of 0.1 M NaCl at $\text{pH} = 7$ ($0.01 \text{ M Na}_2\text{HPO}_4/\text{H}_3\text{PO}_4$). The dissociation of all β -PNA oligomer complexes was shown to be reversible with hysteresis. To prove the influence of NaCl on the pairing stability we also measured the UV and CD spectra for hexamer **15** at $\text{pH} = 7$ without NaCl; this did not significantly change the profile of the melting curve or CD spectra (not shown). In contrast to α -alanyl-PNA^[18], no salt dependence of the pairing complex stability for β -PNA was observed.

The unusually high stability and hyperchromicity of hexamer **15** and pentamer **16** are not only due to double-strand formation but result from higher aggregation. As pointed out in Scheme 4, a β -PNA strand in the extended conformation has two pairing planes. By simultaneous pairing of the Watson–Crick and Hoogsteen pairing planes, aggregation of β -PNA strands is possible, forming band structures based on nucleobase recognition. There are two possibilities for the formation of higher ordered PNA aggregates: (A) either all adenines pair in the Hoogsteen mode or (B) the reversed Watson–Crick and reversed Hoogsteen mode alternate (Scheme 6). In case (A) only one kind of pairing mode is involved and all oligomers have antiparallel strand orientation. In contrast, in case (B) two different alternating pairing modes are required which would be recognized as two steps in the melting curve. Furthermore, all strands should be oriented parallel with all positively charged (at $\text{pH} = 7$) lysine amides directed to the same side. Therefore, we favor case (A) as the most likely structure of

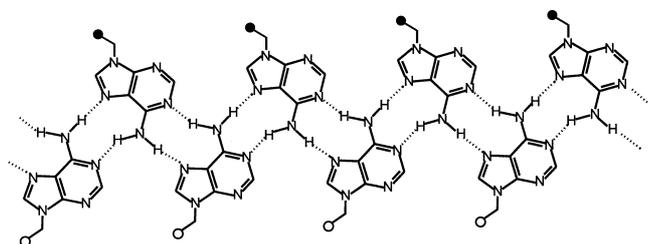
Scheme 5. Melting curves of H-(β -HalA)₆-Lys-NH₂ (**15**), H-(β -HalA)₅-Lys-NH₂ (**16**), H-(β -HalA)₄-Lys-NH₂ (**17**), H-(β -Hal^{7C}A)₆-Lys-NH₂ (**18**), H-(β -Hal^{7C}A)₅-Lys-NH₂ (**19**) and H-(β -Hal^{7C}A)₄-Lys-NH₂ (**20**) (0.01 M Na₂HPO₄/H₃PO₄, pH = 7.0, 0.1 M NaCl, 270 nm)



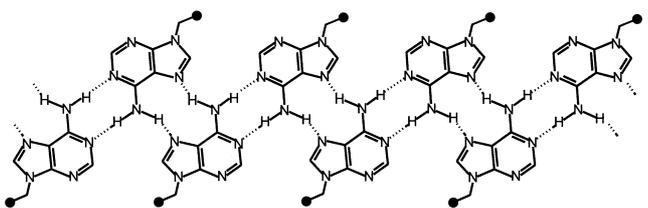
the β -PNA aggregates. Tetramer **17** has a significantly lower stability and hyperchromicity indicating double-strand formation. A–A-pairing double strands in the α -PNA series typically result in a hyperchromicity that is lower than 20%^[5a], whereas aggregation of G–C-pairing α -PNA leads to an enormous increase in hyperchromicity^[5b]. It is quite remarkable that an adenine tetramer still forms a stable pairing complex, therefore providing a strong argument for complexation which cannot result from a 3₁-helix, as is known for β -peptides^{[2][3]}.

Scheme 6. Two possibilities for aggregation of adeninyl- β -homoalanyl-PNA oligomers: (A) all nucleobases pair in the Hoogsteen mode providing alternating backbone orientation; (B) each nucleobase aggregates with the reverse Watson–Crick and the reverse Hoogsteen mode; all strands are oriented alike

A. Hoogsteen mode



B. Alternating reverse Watson–Crick and reverse Hoogsteen mode



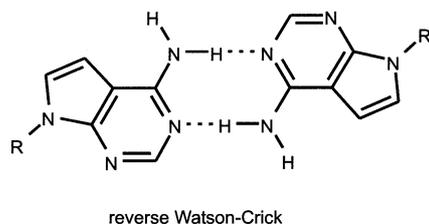
7-Carbaadenine/7-Carbaadenine Pairing of β -PNA Oligomers

To further prove the aggregation model and to obtain information about the A–A-pairing mode we synthesized β -PNAs with 7-carbaadenine instead of adenine as the recognition unit. This modification does not change the geometrical requirements or potential backbone stabilization but excludes pairing of the Hoogsteen side. Therefore, if pairing is found for the 7-carbaadenine oligomers H-(β -Hal^{7C}A)₆-Lys-NH₂ (**18**) and H-(β -Hal^{7C}A)₅-Lys-NH₂ (**19**) [β -Hal^{7C}A = γ -(7-carbaadenine-9-yl)- β -(S)-homoalanine], it would only be possible as a double strand according to the reversed Watson–Crick pairing mode (Scheme 7). The UV melting curves shown in Scheme 5 (D and E) indicate a stability of $T_m = 35^\circ\text{C}$ (24% hyperchromicity, 2 μM) for hexamer **18** and a melting point $T_m = 31^\circ\text{C}$ (14% hyperchromicity, 2 μM) for pentamer **19**. We also measured the tetramer H-(β -Hal^{7C}A)₄-Lys-NH₂ (**20**) (Scheme 5F) which showed $T_m = 28^\circ\text{C}$ (15% hyperchromicity, 2 μM)^[19]. All three 7-carbaadenine oligomers showed melting curves typical for dissociation of a double strand. A difference of one base pair in length results in an increased stability of only 3–4°C. The stability of the adeninyl tetramer **17** ($T_m = 26^\circ\text{C}$, 16% hyperchromicity, 5 μM) is in the same order as the 7-carbaadeninyl β -PNA double strand. Further, the circular dichroism (CD) spectra of the adeninyl tetramer **17** and 7-carbaadeninyl pentamer **19** as well as hexamer **18** (not shown) are similar, especially when compared to the higher organized adeninyl pentamer **16** (Scheme 8). With CD spectroscopy it is possible to distinguish between the pairing complex in which the chromophore (nucleobase) is conformationally fixed in a chiral environment (backbone) and the statistical distribution of a single strand at higher temperatures. Within the same class of backbone a similar

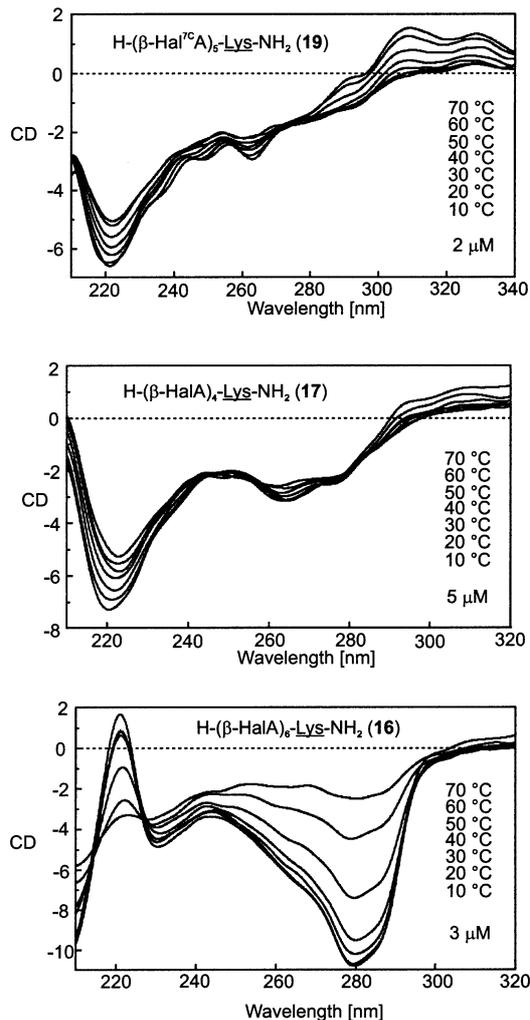
shape observed for CD spectra measured at different temperatures indicates a comparable pairing mode. Therefore, by analogy to the 7-carbaadeninyl oligomers we suggest the pairing mode for the double strand of adeninyl tetramer **17** to be reverse Watson–Crick. It is also noteworthy that the CD effects we observed for the double strands are very small whereas the higher ordered structures of **15** and **16**

show the highest Cotton effect that we have observed so far for alanyl- or homoalanyl-PNA. The small Cotton effects might result from a C_2 -symmetrical pairing complex for the reverse Watson–Crick pairing mode and parallel strand orientation. In contrast, symmetry is lost for the Hoogsteen-pairing higher ordered structure with all strands being antiparallel (Scheme 6A).

Scheme 7. The only possibility for self-pairing of a 7-carbaadenine is the reverse Watson–Crick mode



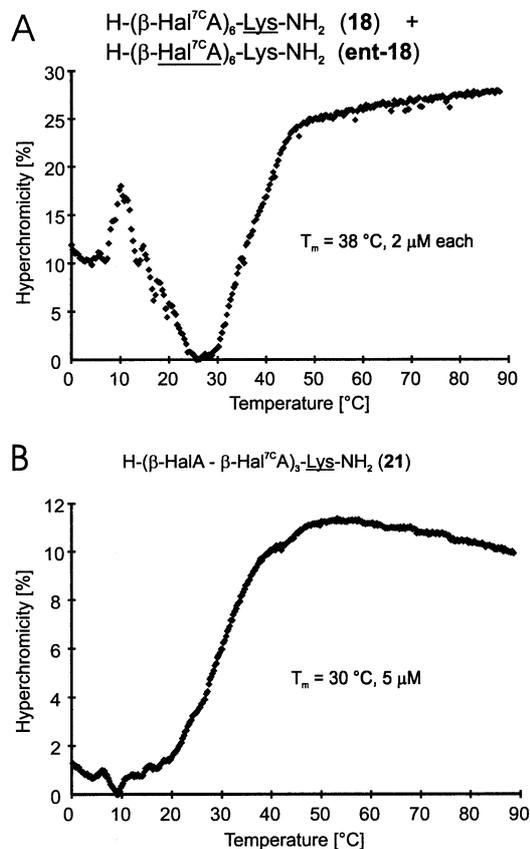
Scheme 8. CD spectra of H-(β -Hal^{7C}A)₅-Lys-NH₂ (**19**), H-(β -HalA)₄-Lys-NH₂ (**17**) and H-(β -HalA)₅-Lys-NH₂ (**16**) (0.01 M Na₂HPO₄/H₃PO₄, pH = 7.0, 0.1 M NaCl, 270 nm); the CD spectra of oligomers **17** and **19** are similar, indicating double-strand formation in the reverse Watson–Crick mode for both; the higher aggregation of β -PNA **16** is also indicated by a drastic change of the CD spectra



Backbone Orientation

A 7-carbaadeninyl- β -PNA oligomer will form a self-pairing complex only as a double strand in the reversed Watson–Crick mode with parallel strand orientation. The equimolar mixture of the enantiomeric oligomers H-(β -Hal^{7C}A)₆-Lys-NH₂ (**18**) and H-(β -Hal^{7C}A)₆-Lys-NH₂ (*ent*-**18**) might also associate in duplexes by forming the reversed Watson–Crick mode but this would require antiparallel oriented backbones. As shown in Scheme 9A, the mixture of the two enantiomers **18** and *ent*-**18** has a UV melting curve with $T_m = 38^\circ\text{C}$ (25% hyperchromicity, 2 μM each). Therefore, the antiparallel strand orientation does not have significantly higher stability than the parallel self-pairing orientation. Since the pairing geometry is the same in both cases, the differentiation between parallel and antiparallel oriented strands might result only from charge separation of the protonated lysine amides in the antiparallel case. The

Scheme 9. Melting curves of the equimolar mixture of H-(β -Hal^{7C}A)₆-Lys-NH₂ (**18**) and H-(β -Hal^{7C}A)₆-Lys-NH₂ (*ent*-**18**) (A) and H-(β -HalA-Hal^{7C}A)₃-Lys-NH₂ (**21**) (0.01 M Na₂HPO₄/H₃PO₄, pH = 7.0, 0.1 M NaCl, 270 nm)



comparable stability of parallel and antiparallel oriented strands is in agreement with base-pair planes being orthogonal to the backbone; this is the only angle which does not effect the strand orientation^[17]. We can further conclude that the influence of the C-terminal lysine amides on the strand orientation is small or negligible.

Alternating Adenyl/7-Carbaadenyl β -Homoalanyl-PNA

The alternating adenyl/7-carbaadenyl oligomer H-(β -HalA-Hal^{7C}A)₃-Lys-NH₂ (**21**) was expected to pair as a double strand because three adenine nucleobases should not be sufficient to form higher ordered structures. Indeed, for oligomer **21**, double-strand formation with a stability of $T_m = 30^\circ\text{C}$ (11% hyperchromicity, 5 μM) was observed (Scheme 9B). Therefore, it is possible to suppress the formation of higher ordered structures by incorporation of 7-carbaadenine which avoids Hoogsteen pairing. Oligomer **21** has a stability 5°C lower compared to oligomer H-(β -Hal^{7C}A)₆-Lys-NH₂ (**18**) which indicates that in a β -homoalanyl-PNA 7-carbaadenine contributes more to hydrogen bonding or stacking than adenine.

Discussion of Pairing Specificities

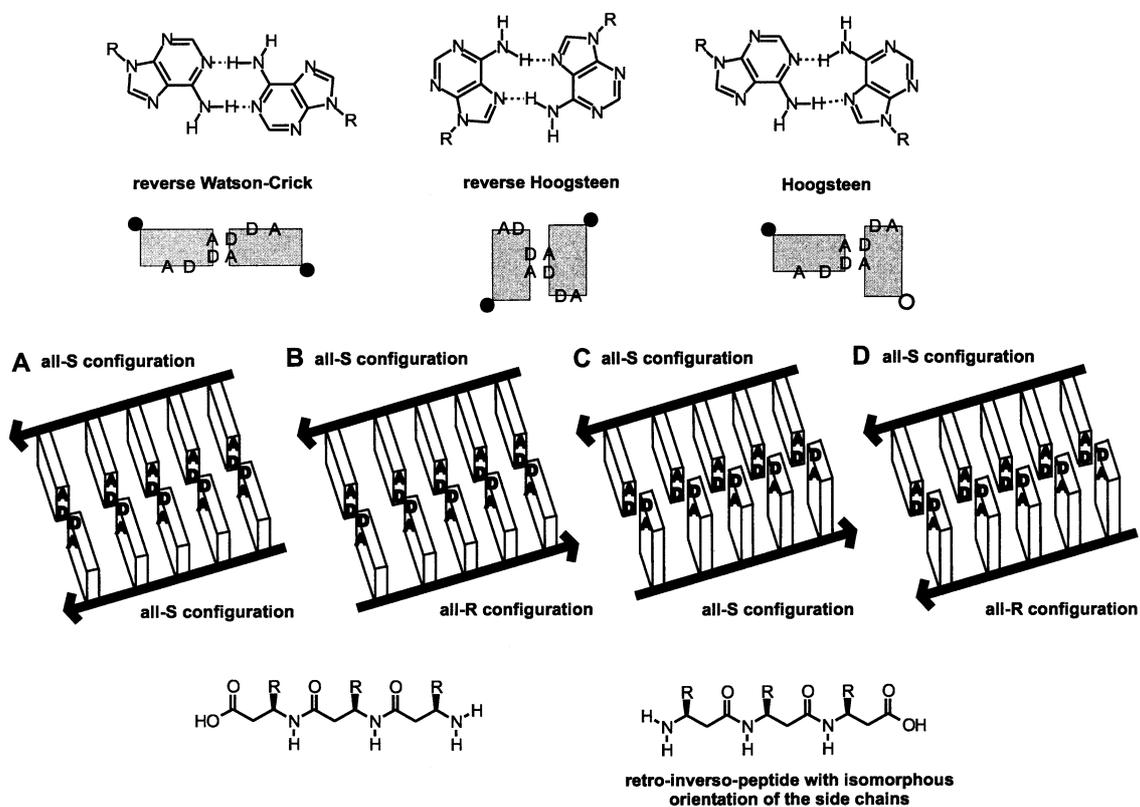
For double-strand formation complementary donor and acceptor positions are required. In the extended conformation of β -homoalanyl-PNA, all purines and all donor/acceptor positions of a single strand are aligned alike.

Therefore, the geometrical requirements of one base pair are also valid for the whole strand. Adenine–adenine self-pairing is possible with three pairing modes (Scheme 10). The reverse Watson–Crick and reverse Hoogsteen pairing modes are both C_2 -symmetrical with both adenines being equal pairing partners. They are interconvertible only by a twist of the strands without changing the strand orientation. In linear self-pairing double strands, the C_2 -symmetrical base pairs, and the respective backbones have the same axis of symmetry. Therefore, the strand orientation of self-pairing β -homoalanyl-PNA strands in the reverse Watson–Crick or reverse Hoogsteen mode is parallel (Scheme 10A).

The two adenine nucleobases in the A–A Hoogsteen mode are not equivalent; one nucleobase pairs on the Watson–Crick side, the other pairs with the Hoogsteen side. The latter requires a reversed orientation of donor/acceptor positions compared to the symmetrical A–A pairing. Therefore, A–A self-pairing in the Hoogsteen mode is possible only with antiparallel strand orientation (Scheme 10C).

In α -peptide chemistry simultaneous altering of the strand orientation (inversion of the sequence) and total inversion of configuration does not change the overall side-chain geometry^[20]. This retro-inverso concept is still valid for β -peptides and β -PNA. Therefore, pairing of β -homoalanyl-PNA in the reverse Watson–Crick mode should also be possible with antiparallel backbone orientation and one

Scheme 10. A β -PNA double strand based on A–A pairing is schematically shown in Scheme 10 with the backbone (arrows for the orientation) and the nucleobases with the donor (D) and acceptor (A) positions indicated; the difference in base pairing between the reverse Watson–Crick or reverse Hoogsteen and the Hoogsteen mode is one adenine unit which changes from the Watson–Crick to the Hoogsteen site by flipping and rotation operations changing the backbone orientation



strand having the inversed configuration (Scheme 10B). Furthermore, a parallel oriented double strand should be preferred for Hoogsteen pairing of an all-(*S*)- with an all-(*R*)-configured backbone (Scheme 10D).

In contrast to β -peptides, the secondary structure of β -homoalanyl peptide nucleic acids is determined by the hydrogen bonds and aromatic π interaction (stacking) of the nucleic acid side chains. Therefore, an extended backbone conformation is stabilized by base pairing and provides an additional motif for β -peptide scaffolds. Compared to α -alanyl-PNA stabilizing in linear double strands in the β -sheet backbone conformation, the β -homoalanyl-PNA oligomers are remarkable because of their uniformly aligned nucleobases. This allows higher aggregation to hydrogen-bonded polymeric structures but also provides stacking of nucleobases in the same orientation and directly on top of each other. Despite a larger base-pair distance, pairing of β -homoalanyl PNA double strands is more stable than that of comparable α -alanyl PNA duplexes which indicates β -homoalanyl-PNA with all canonical nucleobases being a valuable tool for experiments determining nucleobase–amino acid side-chain interactions, intercalation and template-directed oligomerization.

This work was supported by the *Hermann-Schlosser-Stiftung* (Ph. D. fellowship for H. W. S.) and the *Deutsche Forschungsgemeinschaft* (Di 542 2-1). We are grateful to Professor *H. Kessler*, Garching, for generous support.

Experimental Section

General: All reagents were of analytical grade and used as supplied. Solvents were of the highest grade available. – NMR spectra were recorded with a Bruker AC 250, Bruker AMX 500 or Bruker DMX 500. – ESI mass spectra were measured with a TSQ 700 Finnigan spectrometer. – For optical rotation a Perkin-Elmer Polarimeter 241 MC, for elemental analysis a Heraeus EA 415-0 and for melting-point determination a Büchi SMP-20 apparatus was used. – HPLC was done with Beckman System Gold using YMC-Pack ODS, RP-C18, 250 \times 20 mm, 5 μ m, 120 Å for preparation and 250 \times 4.6 mm, 5 μ m, 120 Å for analytical samples. – UV melting curves were measured with a Perkin-Elmer UV/Vis Lambda 10 with Peltier Temperature Programmer PTP 1 and CD spectra were performed with Jasco J-710 with Peltier-Type Temperature Control System PTC-348W. – The optical purity was determined by HPLC analysis of the amino acid dimers obtained with Boc-(*S*)-Ala-OSu. – The oligomer concentration was calculated by taking the extinction coefficient at 90°C as being the sum of the extinction coefficients of the nucleic acid side chains [$\epsilon(\mathbf{1}) = 14000$ at 263 nm]. – The experimental procedures and analytical data of compounds **1**, **9**, **11/13** and oligomers **15**, **16**, **17** are described in the preceding communication^[6].

(*S*)-*N*-tert-Butoxycarbonyl- γ -(6-chloro-7-carba-9-purinyloxy)- β -homoalanine Benzyl Ester (10**):** (*S*)-*N*-Boc- β -homoserine benzyl ester **4** (3.00 g, 9.69 mmol), 6-chloro-7-carbapurine (**6**) (1.49 g, 9.69 mmol), and triphenylphosphane (10.16 g, 38.76 mmol) were dissolved in anhydrous THF (140 ml) and cooled to -78°C . Within 15 min DEAD (6.09 ml, 38.76 mmol) was added and the reaction mixture kept at this temperature for 90 min. After stirring for three days at -20°C the reaction was quenched with water (2 ml) and the solvent evaporated. Purification was done by consecutive flash chromatography (170 g silica gel) with hexanes/ethylacetate (3:2),

chloroform/acetonitrile (9:1), and dichloromethane/acetonitrile gradient (9:1–4:1) to give 1.30 g of **10** (30%) as a colorless solid, m.p. 156–157°C. R_F [chloroform/acetonitrile (9:1)] = 0.46. – $[\alpha]_{589}^{20} = 11.7$ ($c = 1.1$, CH_2Cl_2) – ESI MS; m/z (%): 445.2 (100) $[\text{M} + \text{H}]^+$ – IR (KBr): $\tilde{\nu} = 3365$ cm^{-1} , 2959, 1739, 1683, 1587, 1546, 1530, 1510, 1420, 1354, 1286, 1200, 1134. – ^1H NMR (250 MHz, CDCl_3): $\delta = 1.38$ (s, 9 H, Boc), 2.51–2.63 (m, 2 H, α -H), 4.26–4.45 (m, 3 H, β -H, γ -H), 5.11 (s, 2 H, PhCH_2), 5.41 (d, $J = 8$ Hz, 1 H, BocNH), 6.55 (d, $J = 4$ Hz, 1 H, 7-H), 7.17 (d, $J = 4$ Hz, 1 H, 8-H), 7.28–7.39 (m, 5 H, Ph), 8.53 (s, 1 H, 2-H). – ^{13}C NMR (62 MHz, CDCl_3): $\delta = 28.1$, 36.1, 47.5, 48.1, 66.8, 79.8, 99.8, 104.0, 128.4, 128.5, 128.6, 129.9, 135.3, 150.6, 150.7, 151.4, 152.2, 154.9, 170.8. – $\text{C}_{22}\text{H}_{25}\text{ClN}_4\text{O}_4$ (444.9): calcd. C 59.39, H 5.66, N 12.59; found C 59.27, H 5.55, N 12.51.

(*R*)-*N*-tert-Butoxycarbonyl- γ -(6-chloro-7-carba-9-purinyloxy)- β -homoalanine Benzyl Ester (*ent*-10**):** The synthesis followed the procedure for enantiomer **10** except for the order of adding the reagents. A mixture of the Mitsunobu reagents and 6-chloro-7-carbapurine (**6**) in THF was stirred at -78°C and added to *N*-Boc- β -homoserine benzyl ester (*ent*-**4**) within 5 min at -20°C . Amino acid *ent*-**10** was obtained in 60% yield. The analytical data of *ent*-**10** and **10** are identical except for $[\alpha]_{589}^{20} = -11.9$ ($c = 1.0$, CH_2Cl_2).

(*S*)-*N*-tert-Butoxycarbonyl- γ -(6-azido-7-carba-9-purinyloxy)- β -homoalanine Benzyl Ester (12**):** A suspension of (*S*)-*N*-Boc- γ -(6-chloro-7-carba-9-purinyloxy)- β -homoalanine benzyl ester (**10**) (1.03 g, 2.31 mmol) and sodium azide (2.25 g, 34.67 mmol) in DMF (30 ml) was heated for 12 h at 60°C . After evaporation of the solvent, the residue was suspended in water and extracted with dichloromethane. Purification of the organic phase was done by flash chromatography using 170 g silica gel and hexane/acetone (7:3) gave 643 mg of **12** (62%) against 362 mg recovered starting material which was converted in a second cycle to an additional 297 mg of **12** (28%) next to 38 mg starting material, colorless solid, m.p. 139–140°C. R_F [hexanes/acetone (7:3)] = 0.21. – $[\alpha]_{589}^{20} = 29$ ($c = 1.0$, CHCl_3). – ESI MS; m/z (%): 452.3 (100) $[\text{M} + \text{H}]^+$. – IR (KBr): $\tilde{\nu} = 3357$ cm^{-1} , 3120, 2966, 1742, 1681, 1633, 1531, 1484, 1417, 1393, 1366. – ^1H NMR (250 MHz, CDCl_3): $\delta = 1.28$ (s, 9 H, Boc), 2.52–2.71 (m, 2 H, α -H), 4.35–4.48 (m, 1 H, β -H, γ -H), 4.48–4.62 (m, 2 H, β -H, γ -H), 5.06–5.19 (m, 2 H, PhCH_2), 5.36 (d, $J = 8$ Hz, 1 H, BocNH), 6.41 (d, $J = 4$ Hz, 0.05 H, 7-H azide) 7.02 (d, $J = 4$ Hz, 0.95 H, 7-H tetrazole), 7.09 (m, 0.05 H, 8-H azide), 7.26 (d, $J = 3$ Hz, 0.95 H, 8-H tetrazole), 7.29–7.39 (m, 5 H, Ph), 8.50 (s, 0.05 H, 2-H azide), 9.12 (s, 0.95 H, 2-H tetrazole). – ^{13}C NMR (62 MHz, CDCl_3): $\delta = 28.1$, 35.9, 48.0, 48.4, 66.8, 78.0, 101.9, 103.2, 128.3, 128.4, 128.5, 128.6, 131.2, 135.2, 141.6, 146.6, 154.9, 170.7. – $\text{C}_{12}\text{H}_{25}\text{N}_7\text{O}_4$ (451.5): calcd. C 58.53, H 5.58, N 21.72; found C 58.87, H 5.60, N 21.87.

(*R*)-*N*-tert-Butoxycarbonyl- γ -(6-azido-7-carba-9-purinyloxy)- β -homoalanine Benzyl Ester (*ent*-12**):** The synthesis followed the procedure for enantiomer **12**. The analytical data of *ent*-**12** and **12** are identical except for $[\alpha]_{589}^{20} = -29.7$ ($c = 0.9$, CHCl_3).

(*S*)-*N*-tert-Butoxycarbonyl- γ -(7-carba-9-adeninyloxy)- β -homoalanine (2**):** Palladium oxide hydrate (200 mg, 1.42 mmol) was added to a solution of (*S*)-*N*-Boc- γ -(6-azido-7-carba-9-purinyloxy)- β -homoalanine benzyl ester (**12**) (917 mg, 2.03 mmol) in methanol (80 ml) and acetic acid (400 μ l). After saturation with hydrogen, the reaction mixture was stirred overnight. The precipitated nucleic acid was dissolved in acetonitrile/water (2:3) and separated from the catalyst. Evaporation of the solvent gave a violet solid which was crystallized from hot methanol to yield 409 mg (60%) **2**, colorless solid, m.p. 232–234°C (96% e.e.). – R_F [ethyl acetate/methanol/water/acetic acid (10:1:1:0.5), saturated with NaCl] = 0.54; –

$[\alpha]_{589}^{20} = 38.5$ ($c = 0.8$, DMSO). – ESI MS; m/z (%): 336.1 (100) $[M + H]^+$. – IR (KBr): $\tilde{\nu} = 3420$ cm^{-1} , 2983, 1699, 1680, 1565, 1512, 1394, 1368, 1281, 1247, 1166. – ^1H NMR (500 MHz, $[\text{D}_6]\text{DMSO}$): $\delta = 1.05$ (s, br., 1.5 H, Boc-rotamer), 1.25 (s, br., 7.5 H, Boc), 2.28–2.45 (m, 2 H, α -H), 4.00–4.15 (m, 2 H, γ -H), 4.18–4.29 (m, 1 H, β -H), 6.32–6.40 (m, 0.16 H, 7-H rotamer), 6.50 (d, $J = 3$ Hz, 0.84 H, 7-H), 6.81 (d, $J = 8$ Hz, 0.84 H, BocNH), 6.90 (s, br., 2 H, NH_2), 6.93–6.98 (m, 0.16 H, 8-H rotamer), 7.00 (d, $J = 3$ Hz, 0.84 H, 8-H), 8.01 (s, 1 H, 2-H). – ^{13}C NMR (125 MHz, $[\text{D}_6]\text{DMSO}$): $\delta = 28.1$, 36.9, 46.9, 48.1, 77.7, 98.4, 102.3, 124.4, 149.8, 151.4, 154.7, 157.3, 172.0. – $\text{C}_{15}\text{H}_{21}\text{N}_5\text{O}_4$ (335.4): calcd. C 53.72, H 6.31, N 20.88; found C 53.77, H 6.34, N 20.44.

(*R*)-*N*-*tert*-Butoxycarbonyl- γ -(7-carba-9-adeninyl)- β -homoalanine (*ent*-2): (*R*)-*N*-Boc- γ -(6-azido-7-carba-9-puriny)- β -homoalanine benzyl ester (*ent*-12) (1.17 g, 2.59 mmol) was dissolved in a mixture of dioxane (40 ml), water (25 ml), and acetic acid (2 ml) and reduced by Pd on charcoal (225 mg, 5% Pd on charcoal containing 50.5% water) within 2 d. The precipitated nucle amino acid was separated from the charcoal by dissolving in acetonitrile/methanol (3:2) and subsequent filtration. The solvent was evaporated and the product isolated from the brown residue by crystallization with water/acetonitrile as a white solid giving 661 mg (76%, > 99% e.e.). The analytical data of *ent*-2 and 2 were identical except for $[\alpha]_{589}^{20} = -38.8$ ($c = 0.9$, DMSO).

General Method for SPPS of β -PNA: Oligomerization was performed as a solid-phase peptide synthesis on a 4-methylbenzhydrylamine-(MBHA)-polystyrene resin (50 mg, 15.45 mmol) loaded with (*R*)-lysine(Z)-OH (Z = benzyloxycarbonyl; 0.309 mmol/g) in a small column. For each coupling step an excess of four equivalents of *N*-*tert*-butoxycarbonyl- γ -(9-puriny)- β -homoalanine (77.25 mmol) was used and activated by *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU; 26.40 mg, 69.53 mmol) and *N,N*-diisopropylethylamine (26.3 μl , 154.5 mmol) in DMF (600 μl). After swelling of the resin for 20 min the following procedure was repeated for every nucle amino acid unit: (1) deprotection twice, for 3 min with trifluoroacetic acid/*m*-cresol (95:5; 2 ml); (2) washing five times each with $\text{CH}_2\text{Cl}_2/\text{DMF}$ (1:1; 2 ml) and pyridine (2 ml); (3) coupling step, 40–50 min gentle moving of the reaction column; (4) washing three times each with $\text{CH}_2\text{Cl}_2/\text{DMF}$ (1:1; 2 ml), DMF/piperidine (95:5; 2 ml), and $\text{CH}_2\text{Cl}_2/\text{DMF}$ (1:1; 2 ml). Finally, the β -PNA was washed twice with TFA (2 ml) and cleaved from the solid support within 1 h using 1.6 ml trifluoroacetic acid/trifluoromethanesulfonic acid/*m*-cresol (8:1:1). The dark brown solution was concentrated to 400 μl , and the β -PNA precipitated with diethyl ether (5 ml) as a white solid. The β -PNA was separated using a centrifuge, followed by purification with HPLC (RP-C18). The yield of each coupling step was estimated from HPLC to be higher than 97%.

H-[(*S*)- β -Hal $^{\text{7C}}\text{A}$] $_6$ -(*R*)-Lys-NH $_2$ (18): The synthesis followed the general method for SPPS. – ESI MS; m/z (%): 1470.6 (12) $[M + \text{Na}]^+$, 725.1 (100) $[M + 2 H]^2+$. – HPLC: 27.0 min, gradient 5–20% acetonitrile in 30 min. – ^1H NMR (500 MHz, D_2O): $\delta = 1.32$ –1.49 (m, 2 H, H-Lys), 1.58–1.83 (m, 4 H, H-Lys), 2.12–2.25 (m, 2 H, α -H), 2.26–2.46 (m, 7 H, α -H), 2.47–2.59 (m, 2 H, α -H), 2.69–2.79 (m, 1 H, α -H), 2.95 (t, $J = 8$ Hz, 2 H, ϵ -H-Lys), 3.28–3.43 (m, 3 H, β -H, γ -H), 3.54–3.62 (m, 1 H, β -H, γ -H), 3.60 (m, 3 H, β -H, γ -H), 3.78–3.87 (m, 2 H, β -H, γ -H), 3.88–3.96 (m, 1 H, β -H, γ -H), 4.10–4.19 (m, 1 H, γ -H), 4.19 (m, 1 H, α -H-Lys), 4.23–4.35 (m, 1 H, γ -H), 4.36–4.55 (m, 4 H, γ -H), 4.55–4.62 (1 H, γ -H), 4.78–4.89 (m, 1 H, γ -H), 6.60–6.75 (m, 5 H, 7-H), 6.89 (d, $J = 4$ Hz, 1 H, 7-H), 7.09 (m, 2 H, 8-H), 7.12 (d, $J = 3$ Hz, 1

H, 8-H), 7.19 (d, $J = 3$ Hz, 1 H, 8-H), 7.23 (d, $J = 3$ Hz, 1 H, 8-H), 7.35 (d, $J = 3$ Hz, 1 H, 8-H), 8.13 (s, 1 H, 2-H), 8.14 (s, 1 H, 2-H), 8.15 (m, 2 H, 2-H), 8.17 (m, 2 H, 2-H).

H-[(*R*)- β -Hal $^{\text{7C}}\text{A}$] $_6$ -(*S*)-Lys-NH $_2$ (*ent*-18): The synthesis followed the general method for SPPS and the spectroscopic data are in agreement with those for enantiomer 18.

H-[(*S*)- β -Hal $^{\text{7C}}\text{A}$] $_5$ -(*R*)-Lys-NH $_2$ (19): The synthesis followed the general method for SPPS. – ESI MS; m/z (%): 1231.6 (100) $[M + H]^+$, 616.6 (95) $[M + 2 H]^2+$. – HPLC: 25.2 min, gradient 5–20% acetonitrile in 30 min. – ^1H NMR (500 MHz, D_2O): $\delta = 1.32$ –1.49 (m, 2 H, H-Lys), 1.60–1.72 (m, 3 H, H-Lys), 1.73–1.82 (m, 1 H, H-Lys), 2.13–2.45 (m, 7 H, α -H), 2.48–2.59 (m, 2 H, α -H), 2.70–2.79 (m, 1 H, α -H), 2.95 (t, $J = 8$ Hz, 2 H, ϵ -H-Lys), 3.20 (m, 2 H, β -H, γ -H), 3.49 (m, 1 H, β -H, γ -H), 3.56 (m, 1 H, β -H, γ -H), 3.67 (m, 1 H, β -H, γ -H), 3.70–3.82 (m, 2 H, β -H, γ -H), 3.88 (m, 1 H, β -H, γ -H), 4.03–4.11 (m, 1 H, γ -H), 4.18 (m, 1 H, α -H-Lys), 4.23–4.33 (m, 1 H, γ -H), 4.35–4.45 (m, 2 H, γ -H), 4.45–4.53 (m, 1 H, γ -H), 4.53–4.62 (m, 1 H, γ -H), 4.78–4.88 (m, 1 H, γ -H), 6.58–6.62 (m, 2 H, 7-H), 6.63 (d, $J = 3$ Hz, 1 H, 7-H), 6.64 (d, $J = 3$ Hz, 1 H, 7-H), 6.76 (d, $J = 3$ Hz, 1 H, 7-H), 7.06 (m, 2 H, 8-H), 7.13 (d, $J = 3$ Hz, 1 H, 8-H), 7.21 (d, $J = 4$ Hz, 1 H, 8-H), 7.35 (d, $J = 4$ Hz, 1 H, 8-H), 8.12 (m, 2 H, 2-H), 8.16 (m, 3 H, 2-H).

H-[(*R*)- β -Hal $^{\text{7C}}\text{A}$] $_4$ -(*S*)-Lys-NH $_2$ (20): The synthesis followed the general method for SPPS. – ESI MS; m/z (%): 1036.6 (5) $[M + \text{Na}]^+$, 508.1 (23) $[M + 2 H]^2+$, 339.2 (100) $[M + 3 H]^3+$. – HPLC: 22.1 min, gradient 5–25% acetonitrile in 30 min. – ^1H NMR (500 MHz, D_2O): $\delta = 1.29$ –1.50 (m, 2 H, H-Lys), 1.55–1.88 (m, 4 H, H-Lys), 2.13–2.25 (m, 1 H, α -H), 2.25–2.45 (m, 4 H, α -H), 2.48–2.65 (m, 2 H, α -H), 2.68–2.80 (m, 1 H, α -H), 2.95 (t, $J = 7$ Hz, 2 H, ϵ -H-Lys), 3.41 (m, 1 H, β -H), 3.52 (m, 1 H, β -H), 3.66 (m, 1 H, β -H), 3.77 (m, 1 H, β -H), 3.80–3.95 (m, 3 H, γ -H), 4.05–4.21 (m, 2 H, α -H-Lys, γ -H), 4.22–4.32 (m, 1 H, γ -H), 4.32–4.49 (m, 2 H, H- γ), 4.50–4.60 (m, 1 H, γ -H), 4.77–4.95 (m, 1 H, γ -H), 6.60–6.75 (m, 3 H, 7-H), 6.80 (d, $J = 3$ Hz, 1 H, 7-H), 7.11 (d, $J = 3$ Hz, 1 H, 8-H), 7.15 (d, $J = 3$ Hz, 1 H, 8-H), 7.22 (d, $J = 3$ Hz, 1 H, 8-H), 7.56 (d, $J = 3$ Hz, 1 H, 8-H), 8.17 (s, 1 H, 2-H), 8.19 (s, 1 H, 2-H), 8.20 (s, 1 H, 2-H), 8.21 (s, 1 H, 2-H).

H-[(*S*)- β -HalA-(*S*)- β -Hal $^{\text{7C}}\text{A}$] $_3$ -(*R*)-Lys-NH $_2$ (21): The synthesis followed the general method for SPPS. – ESI MS; m/z (%): 1451.6 (34) $[M + H]^+$, 726.7 (100) $[M + 2 H]^2+$. – HPLC: 12.3 min, gradient 10–20% acetonitrile in 30 min. – ^1H NMR (500 MHz, D_2O): $\delta = 1.33$ –1.50 (m, 2 H, H-Lys), 1.59–1.82 (m, 4 H, H-Lys), 2.16–2.49 (m, 8 H, α -H), 2.50–2.60 (m, 2 H, α -H), 2.68–2.80 (m, 2 H, α -H), 2.95 (t, $J = 7$ Hz, 2 H, ϵ -H-Lys), 3.58 (m, 1 H, β -H, γ -H), 3.62–3.80 (m, 3 H, β -H, γ -H), 3.81–4.10 (m, 6 H, β -H, γ -H), 4.17 (m, α -H-Lys), 4.19–4.32 (m, 2 H, β -H, γ -H), 4.33–4.70 (m, 7 H, β -H, γ -H), 6.60–6.71 (m, 3 H, 7-H $^{\text{7C}}\text{A}$), 7.09 (d, $J = 3$ Hz, 1 H, 8-H $^{\text{7C}}\text{A}$), 7.19 (d, $J = 3$ Hz, 1 H, 8-H $^{\text{7C}}\text{A}$), 7.31 (d, $J = 3$ Hz, 1 H, 8-H, $^{\text{7C}}\text{A}$), 8.05 (s, 2 H, 2-H, 2-H $^{\text{7C}}\text{A}$, 8-H), 8.11 (s, 2 H, 2-H, 2-H $^{\text{7C}}\text{A}$, 8-H), 8.14 (s, 1 H, 2-H, 2-H $^{\text{7C}}\text{A}$, 8-H), 8.16 (s, 1 H, 2-H, 2-H $^{\text{7C}}\text{A}$, 8-H), 8.21 (s, 3 H, 2-H, 2-H $^{\text{7C}}\text{A}$, 8-H).

General Method for UV Melting Curves and CD Spectroscopy: The oligomers (2–5 μM) were dissolved in an $\text{Na}_2\text{HPO}_4/\text{H}_3\text{PO}_4$ buffer (pH = 7.0, 0.01 M) containing NaCl (0.1 M) and placed in a UV cell (10 mm). For UV melting curves the following temperature program was used to control the heating block: 90°C \rightarrow –2°C (90 min) \rightarrow –2°C (10 min) \rightarrow 90°C (190 min) \rightarrow –2°C (190 min) \rightarrow –2°C (10 min) \rightarrow 90°C (190 min) \rightarrow –2°C (190 min). The temperature for UV spectra was measured directly in the solution and

for CD spectra the temperature of the heating block was determined.

- [1] [1^a] U. Koert, *Angew. Chem.* **1997**, *109*, 1922; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1836. — [1^b] S. Borman, *Chem. Eng. News* **1997**, *June 16*, 32. — [1^c] B. L. Iverson, *Nature* **1997**, *385*, 113.
- [2] [2^a] D. Seebach, M. Overhand, F. N. M. Kühnle, B. Martinoni, L. Oberer, U. Hommel, H. Widmer, *Helv. Chim. Acta* **1996**, *79*, 913. — [2^b] D. Seebach, P. E. Ciceri, M. Overhand, B. Jaun, D. Rigo, L. Oberer, U. Hommel, R. Amstutz, H. Widmer, *Helv. Chim. Acta* **1996**, *79*, 2043. — [2^c] J. L. Matthews, M. Overhand, F. N. M. Kühnle, P. E. Ciceri, D. Seebach, *Liebigs Ann.* **1997**, *1371*. — [2^d] T. Hintermann, D. Seebach, *Chimia* **1997**, *51*, 244. — [2^e] G. Guichard, D. Seebach, *Chimia* **1997**, *51*, 315. — [2^f] X. Daura, W. F. van Gunsteren, D. Rigo, B. Jaun, D. Seebach, *Chem. Eur. J.* **1997**, *3*, 1410. — [2^g] T. Hintermann, D. Seebach, *Synlett* **1997**, 437. — [2^h] D. Seebach, K. Gademann, J. V. Schreiber, J. L. Matthews, T. Hintermann, B. Jaun, *Helv. Chim. Acta* **1997**, *80*, 2033. — [2ⁱ] D. Seebach, J. L. Matthews, *J. Chem. Soc., Chem. Commun.* **1997**, 2015.
- [3] [3^a] D. H. Appella, L. A. Christianson, I. L. Karle, D. R. Powell, S. H. Gellman, *J. Am. Chem. Soc.* **1996**, *118*, 13071. — [3^b] D. H. Appella, L. A. Christianson, D. A. Klein, D. R. Powell, X. Huang, J. J. Barchi Jr., S. H. Gellman, *Nature* **1997**, *387*, 381.
- [4] S. Marqusee, R. L. Baldwin, *Proc. Natl. Acad. Sci. USA* **1987**, *84*, 8898.
- [5] [5^a] U. Diederichsen, *Angew. Chem.* **1996**, *108*, 458; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 445. — [5^b] U. Diederichsen, *Angew. Chem.* **1997**, *109*, 1966; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1886. — [5^c] U. Diederichsen, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1743. — [5^d] U. Diederichsen, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 145. — [5^e] U. Diederichsen, H. W. Schmitt, *Tetrahedron Lett.* **1996**, *37*, 475.
- [6] U. Diederichsen, H. W. Schmitt, *Angew. Chem.* **1998**, *110*, 312; *Angew. Chem. Int. Ed.* **1998**, *37*, 302.
- [7] [7^a] E. Juaristi, D. Quintana, J. Escalante, *Aldrichim. Acta* **1994**, *27*, 3. — [7^b] D. C. Cole, *Tetrahedron Lett.* **1994**, *50*, 9517. — [7^c] G. Cardillo, C. Tomasini, *Chem. Soc. Rev.* **1996**, 117. — [7^d] J. Podlech, D. Seebach, *Angew. Chem.* **1995**, *107*, 507; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 471. — [7^e] J. Podlech, D. Seebach, *Liebigs Ann.* **1995**, 1217. — [7^f] N. N. Romanova, A. G. Gravis, Y. G. Bundel, *Russ. Chem. Rev.* **1996**, *65*, 1083.
- [8] [8^a] C. G. Overberger, J. Y. Chang, *Tetrahedron Lett.* **1989**, *30*, 51. — [8^b] M. L. Peterson, R. Vince, *J. Med. Chem.* **1991**, *34*, 2787. — [8^c] T. F. Jenny, N. Previsani, S. A. Benner, *Tetrahedron Lett.* **1991**, *32*, 7029. — [8^d] T. F. Jenny, K. C. Schneider, S. A. Benner, *Nucleosides Nucleotides* **1992**, *11*, 1257. — [8^e] A. Toyota, N. Katagiri, C. Kaneko, *Synth. Commun.* **1993**, *23*, 1295. — [8^f] M. R. Harnden, A. Parkin, M. J. Parratt, R. M. Perkins, *J. Med. Chem.* **1993**, *36*, 1343. — [8^g] A. Bouali, D. F. Ewing, G. Mackenzie, *Nucleosides Nucleotides* **1994**, *13*, 491.
- [9] G. Kokotos, *Synthesis* **1990**, 299.
- [10] [10^a] J. Davoll, *J. Am. Chem. Soc.* **1951**, *73*, 3174. — [10^b] J. Davoll, *J. Chem. Soc.* **1960**, 131.
- [11] M. Ho, J. K. K. Chung, N. Tang, *Tetrahedron Lett.* **1993**, *34*, 6513.
- [12] [12^a] F. R. Benson, T. W. Hartzel, E. A. Otten, *J. Am. Chem. Soc.* **1954**, *76*, 1858. — [12^b] Z. Kazimierczuk, H. B. Cottam, G. R. Revankar, R. K. Robins, *J. Am. Chem. Soc.* **1994**, *106*, 6379.
- [13] The N-9 constitution of the isolated regioisomer was proved by HMQC and HMBC NMR experiments [H. Kessler, S. Seip in *Two-Dimensional NMR Spectroscopy*, 2nd ed. (Eds.: W. R. Croasmun, R. M. K. Carlson), VCH, Weinheim, **1994**, p. 619].
- [14] C. Temple, C. L. Kussner, J. A. Montgomery, *J. Org. Chem.* **1966**, *31*, 2210.
- [15] (*R*)-Lysine amide was introduced for solubility reasons. The (*R*) configuration was chosen by analogy to α -alanyl-PNA providing all side chains oriented on the same side of the backbone in the extended conformation.
- [16] [16^a] W. Saenger, *Principles of Nucleic Acid Structure*, Springer Verlag, New York, **1983**. — [16^b] I. Berger, C. Kang, A. Fredian, R. Ratliff, R. Moyzis, A. Rich, *Nat. Struct. Biol.* **1995**, *2*, 416. — [16^c] K. J. Baejens, H. L. De Bondt, A. Pardi, S. R. Holbrook, *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 12851.
- [17] [17^a] J. Hunziker, H.-J. Roth, M. Böhringer, A. Giger, U. Diederichsen, M. Göbel, R. Krishnan, B. Jaun, C. Leumann, A. Eschenmoser, *Helv. Chim. Acta* **1993**, *76*, 259. — [17^b] K. Groebke, J. Hunziker, W. Fraser, L. Peng, U. Diederichsen, K. Zimmermann, A. Holzner, C. Leumann, A. Eschenmoser, *Helv. Chim. Acta* **1998**, *81*, 375. — [17^c] S. Pitsch, S. Wendeborn, B. Jaun, A. Eschenmoser, *Helv. Chim. Acta* **1993**, *76*, 2161.
- [18] U. Diederichsen, unpublished results.
- [19] The double-strand formation of 7-carbaadeninyl tetramer **20** was much slower than the others when cooled to 0°C. Therefore the UV melting curve was measured with a different temperature program [80°C → -2°C (60 min) → -2°C (270 min) → 80°C (300 min) → -2°C (180 min) → -2°C (270 min) → 80°C (300 min) → -2°C (180 min)].
- [20] [20^a] V. Prelog, H. Gerlach, *Helv. Chim. Acta* **1964**, *47*, 2288. — [20^b] H. Gerlach, J. A. Owtschinnikow, V. Prelog, *Helv. Chim. Acta* **1964**, *47*, 2294. — [20^c] M. M. Shemyakin, Y. A. Ovchinnikov, V. T. Ivanov, *Angew. Chem.* **1969**, *81*, 523, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 492. — [20^d] M. Chorev, M. Goodman, *Acc. Chem. Res.* **1993**, *26*, 266.

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