Intramolecular Versus Intermolecular Induction of Helical Handedness in Pyridinedicarboxamide Oligomers

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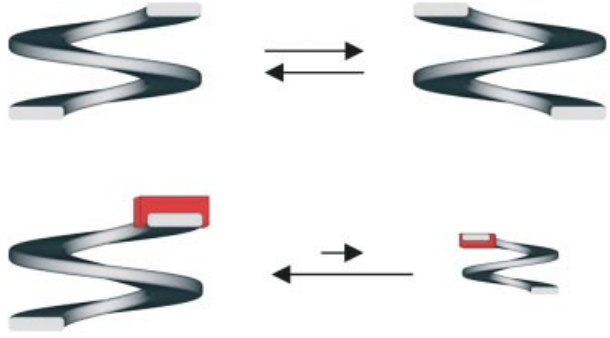
A new convergent synthetic scheme has been developed to prepare oligoamides of 2,6-diaminopyridine and 4-decyloxy-2,6-pyridinedicarboxylic acid. These compounds adopt stable single helical conformations in solution. NMR and circular dichroism studies show that intramolecular and intermolecular chiral induction of handedness in these helices is possible. Intramolecular induction is effected by attaching a single chiral group to the end of an oligomer. Intermolecular induction results from various noncovalent interactions between chiral carboxylic or sulfonic acids and the terminal residues of the oligoamides. Intramolecular induction appears to be more efficient than intermolecular induction. When both effects compete, intramolecular induction prevails.

Introduction

Numerous oligomers and polymers spontaneously adopt right- or left-handed helical conformations.[1–4] When the energy barrier between these two forms can be overcome under experimental conditions, an equilibrium is formed. In the absence of any chirality within the helices or in the surrounding medium, the proportions of the two forms are expected to be equal. However, when the helices interact with chiral groups, the right- and left-handed conformations become diastereomeric. Thus, the equilibrium may be shifted in one direction or the other and a particular handedness may be induced (Scheme 1).[1,5]

A remarkable aspect of the chiral induction of helical handedness is that it is often associated with chiral amplification.[5,6] For an effective induction to take place, it need not occur at each and every monomer of the helix. Instead, it may simply occur at a small fraction of the monomers and be propagated along the helical chain until any factor, for example local uncoiling, interrupts the continuity of the helix.[5,7] Recalling the analogy proposed by Green et al., the monomers that impose a helical bias may be likened to sergeants, and the monomers that follow this bias to soldiers.[8] Thus, the handedness of many monomers may be biased by just a small quantity of a chiral substance or by a nearly − but not perfectly − racemic compound. The initial weak chiral stimulus is amplified by the polymer and may be easily detected by, for example, intense circular dichroism bands that arise from chromophores in the helical chain. Such phenomena have already been applied to the detection, assignment, and quantification of chirality.[6,9]



Scheme 1. Schematic representation of the equilibria formed between enantiomeric left- and right-handed helices (top), and between diastereomeric left- and right-handed helices (bottom). The chiral moiety in red may be covalently or noncovalently bound to the helix. The bottom equilibrium has been arbitrarily shifted in favor of the left-handed helix.

Other important aspects of the chiral induction of helical handedness involve chirality switching and memorizing. For instance, a right-handed bias induced in a helical polymer by a group of given chirality may be converted to a left-handed bias by changing the polarity of the solvent or the temperature,[10–14] or even by more specific methods such as the binding of nonchiral guest molecules[15] or by irradiation with unpolarized[16–19] or circularly polarized light.[20,21] Consequently, a small change in the environment of the helical chain may give rise to a large chiroptical signal inversion, a feature that may be of use in some optical devices. Chiral induction in helices has also been associated with spectacular memory effects. Under particular conditions, the handedness induced by a chiral stimulus may be memorized even after the stimulus has been retrieved.[6,22]

Previously, we reported on the ability of oligoamides of 2,6-diaminopyridine and 2,6-pyridinedicarboxylic acid to

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fold into helices that are stabilized by intramolecular aromatic–aromatic interactions and by both attractive and repulsive electrostatic interactions involving either the amidic hydrogen or oxygen atom on the one hand and the adjacent pyridine′s nitrogen atoms and protons on the other.[23–26] Remarkably, these single helices can extend like springs and wind around each other to form double helical molecular duplexes.[23,27,28] The single helices have been characterized in the solid state and even relatively short oligomers (15 pyridine units or less) have been shown to be remarkably stable in a number of nonpolar and polar solvents, for example, chloroform, toluene, DMSO, and water, over a wide temperature range. The stability of these structures and their ability to remain folded in helices allows us to speculate that polymers in this series should have a consistent handedness over many helical turns. Given the interest in chiral induction mentioned above, we have investigated whether it is possible to bias helical handedness in these compounds through intramolecular and intermolecular interactions. We briefly mentioned this possibility in a previous communication[26] and here we give the first full report of our results. For the intramolecular induction of helical handedness, we prepared octamer **1**, which has a chiral (*R*)- or (*S*)-phenethylamino group (Figure 1). For the intermolecular induction of helical handedness, we used nonchiral heptamer **2** and studied its behavior in the presence of various chiral acids **3**–**6**.

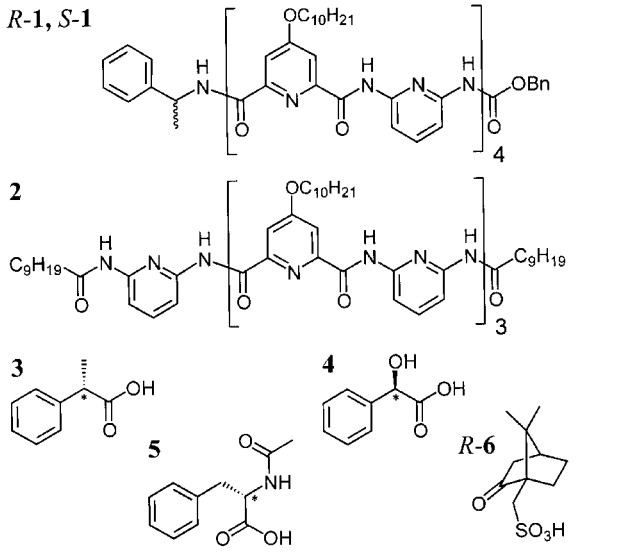
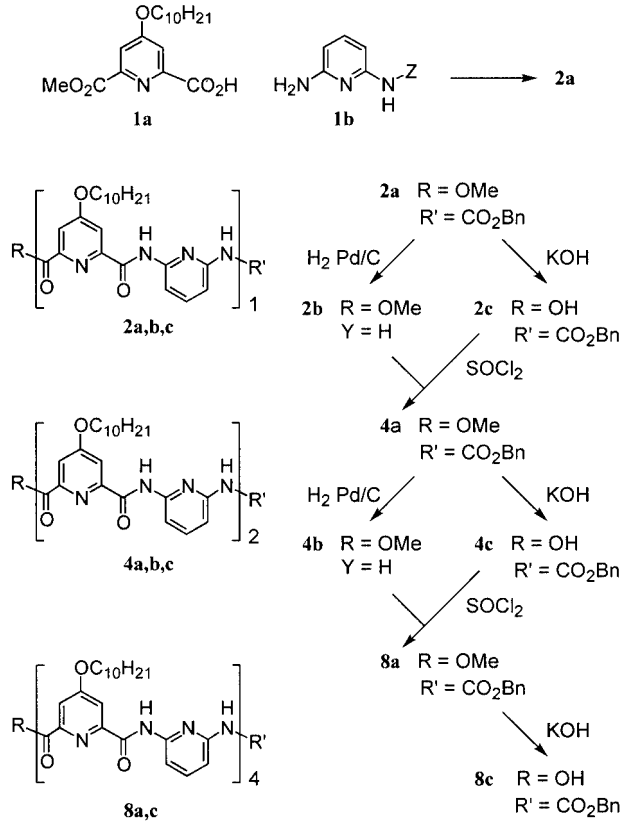


Figure 1. Structures of compounds **1**–**6**.

metrization of the diamine and diacid monomers. For clarity, the following synthetic intermediates are labeled according to the number of pyridine rings that they contain. As we recently reported,[28] monoester **1a** can be obtained in 85% yield from the corresponding diester and one equivalent of KOH (Scheme 2). Similarly, the mono-amine monobenzyl carbamate **1b** can be prepared from commercially available 2,6-diaminopyridine and benzyl chloroformate in 84% yield. Activation of **1a** to its acid chloride with $SOCl_2$ and coupling with amine **1b** yields dimer **2a**. This compound can be quantitatively deprotected at its C-terminus by saponification and at its N-terminus by hydrogenolysis of the benzyl carbamate to yield dimers **2c** and **2b**, respectively. After activation of acid **2c** with $SOCl_2$, these two dimers can be coupled to yield tetramer **4a** (Scheme 2). Starting from **4a**, another cycle of deprotection, activation with $SOCl_2$, and coupling gives octamer **8a**, which can in turn be saponified, activated using HBTU and coupled to (*R*)- or (*S*)-phenethylamine following standard procedures[29] to yield (*R*)-**1** and (*S*)-**1**.



Scheme 2.

Results and Discussion

Synthesis

The synthesis of the symmetrical heptamer **2** has been described previously.[24] It follows a highly convergent strategy, but involves a low-yielding late desymmetrization step. On the other hand, octamer **1** was prepared according to a new scheme[28] based on an early and high-yielding desym-

The structure of dimer **2a** was characterized in the solid state by single-crystal X-ray diffraction analysis. Figure 2 shows that **2a** has a planar crescent-like shape and illustrates the conformational preferences of these compounds at each pyridine–amide linkage. The amidic carbonyl moiety diverges away from the neighboring endocyclic nitrogen atoms of the pyridine moiety, whereas the amidic proton converges towards them. Upon increasing the length of this molecular strand, the crescent shape will extend until a ste-

ric clash forces the two ends of the strand to deviate from planarity and adopt a helical conformation. The helices are characterized by a pitch equal to the thickness of one aromatic ring (3.45 Å) and by a curvature of 4.5 units per turn.[23–25] Heptamer **2** thus consists of one-and-a-half helical turns and octamer **1** of almost two turns.

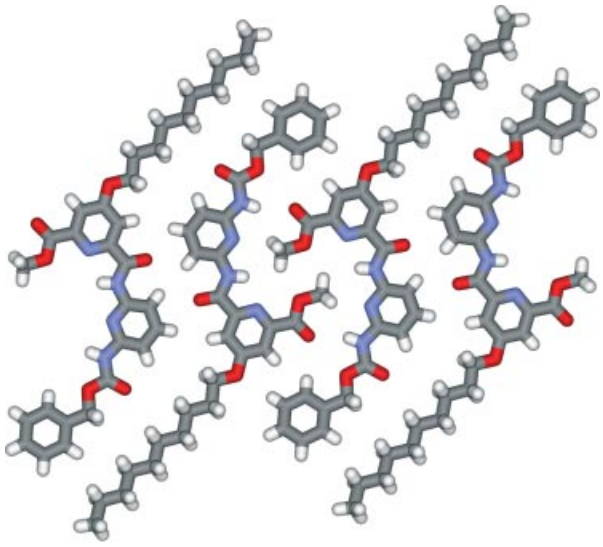


Figure 2. Crystal structure and molecular packing of **2a**.

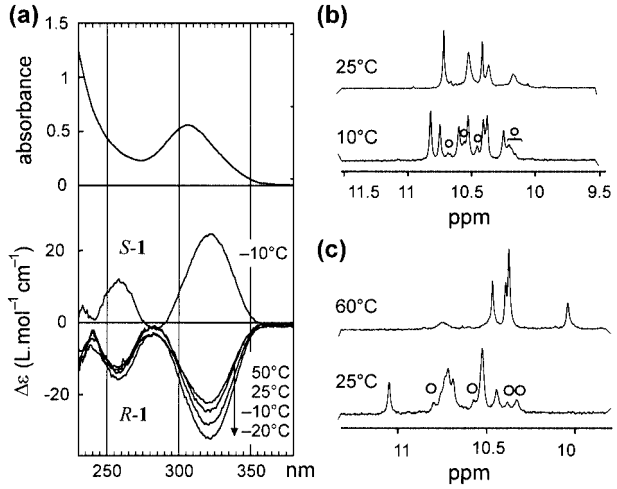


Figure 3. (a) Electronic absorption and CD spectra of 1 M solutions of (*S*)- and (*R*)-**1** in $CHCl_3$ at various temperatures. Spectra could not be measured below 210 nm because the oligomers are not soluble in solvents that do not absorb at these wavelengths. Part of the ^1H NMR (400 MHz) spectra of (*R*)-**1** showing the amide resonances in (b) $CDCl_3$ and (c) $[D_8]$toluene. The circles indicate signals from the minor helical diastereomer.

Intramolecular Chiral Induction

The chiral induction in octamer **1**, which has one covalently linked chiral group, was demonstrated by circular dichroism spectroscopy (CD). In contrast to the silent CD spectra of helical oligomers that have no chiral groups, the spectrum of (*R*)-**1** features two intense negative bands at 270 ($\Delta\varepsilon$ = 12 $L\,mol^{-1}\,cm^{-1}$) and 322 nm ($\Delta\varepsilon$ = 21 $L\,mol^{-1}\,cm^{-1}$) allied to the electronic transitions of the pyridine chromophores [see (a) in Figure 3]. For comparison, when the phenethylamine moiety is appended to a very short oligomer such as dimer acid **2c**, which is too short to be helical, no CD is observed above 250 nm. Thus, in octamer **1**, intramolecular interactions between the single chiral phenethylamino group and the helix differ in the right-handed (*R*-P) and in the left-handed (*R*-M) helical diastereomers leading to different stabilities of the P and M helices in solution. Conversely, the CD spectrum of (*S*)-**1** features two positive bands at the same wavelengths showing that, as expected, the sign of chiral induction is reversed upon inverting the chirality at the asymmetric carbon.

The sign of the CD bands alone does not allow us to assign the favored and unfavored handedness to the P or M helix, as was already the case for related oligomers derived from quinoline.[29] We looked at molecular models of the two diastereoisomers of (*R*)-**1** but there is no obvious difference between them to indicate which should be the most stable in solution.

The intensities of the induced CD bands increase by around 30% upon decreasing the temperature from 50 to –20 °C [see (a) in Figure 3]. This may be a result of more efficient chiral induction at low temperatures which causes the difference in the population of the P-**1** and M-**1** diastereoisomers to increase. It may also arise without a change in the diastereoisomer populations, for example, when the helices adopt a more consistently folded helical conformation at low temperatures.

The NMR spectra have allowed us to evaluate the extent of chiral induction. At 25 °C, the ^1H NMR spectrum of a 1 mM solution of (*R*)-**1** shows one set of slightly broadened signals. Upon cooling to 10 °C, the equilibrium between the right- and left-handed helices slows on the NMR time scale, and the signals split into two sets of different intensities which can be assigned to helices with favored and unfavored handedness [see (b) in Figure 3]. The two sets of signals partly overlap and integration is not very accurate. Nevertheless, the ratio of the two diastereoisomers can be estimated to be 70:30 which corresponds to a diastereomeric excess of 40%. Upon cooling further to –20 °C (not shown), the diastereomeric excess does not change significantly. This shows that the variation in the intensity of the CD bands with temperature in this solvent is not due to a variation in the efficiency of chiral induction, but presumably arises from slight changes in the helical conformation of the oligomers, for example, better folding at a lower temperature. In $[D_8]$toluene, the same two sets of signals are observed even at 25 °C and coalesce upon heating. This shows that the rate of helix inversion is lower in this solvent than in $CDCl_3$. On the other hand, the diastereomeric excess in toluene is identical to that observed in $CDCl_3$.

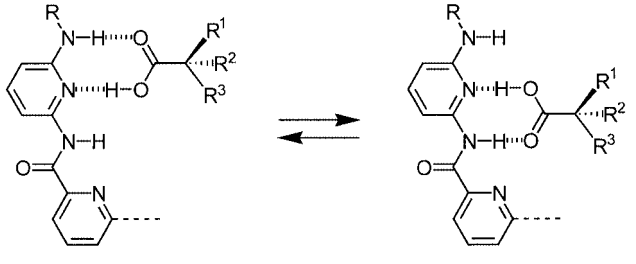
These NMR spectra also show that a 1 mM solution of octamer **1** in $CDCl_3$ or $[D_8]$toluene shows no sign of double helix formation between –20 and 60 °C.[23,27,28] The induced handedness observed in **1** in the CD and NMR spectra con-

cerns only its single helical form. Duplex formation does occur at higher concentrations and/or lower temperatures. However, the dimerization constant could not be measured accurately because the signals of the monomers P-**1** and M-**1** overlap with the numerous signals that arise from the head-to-head and head-to-tail forms of dimers P-$\mathbf{1}_2$ and M-$\mathbf{1}_2$. For comparison, the dimerization constant of octamer ester **8a** is estimated to be less than 5 L mol^{-1} in $CHCl_3$ at 25 °C.

Intermolecular Chiral Induction

The equilibrium between a right- and left-handed helix may be shifted when chiral molecules interact noncovalently with the helices. For example, strong handedness induction has been observed when multiple chiral molecules interact with helical polymers such as polyacetylene,[6] polyaniline,[30] polyguanidine,[31] or polyisocyanate.[32] The inclusion of a chiral molecule in the helix hollow of oligophenylenes-acetylenes also results in such a chiral bias.[33,34] A combination of chiral induction and amplification has been demonstrated in nonchiral α-helical peptides in which the interaction of a single chiral carboxylic acid with the N-terminal ammonium leads to an induction of helical handedness.[35]

In the case of the pyridinedicarboxamide oligomers, we suggested that chiral induction may occur by well-characterized hydrogen bonding between carboxylic acids and acylaminopyridines.[36] Binding to diacylaminopyridine units residing at the center of helical pyridinedicarboxamide oligomers should be disfavored because the amidic protons of these units are already hydrogen bonded to the pyridine's nitrogen atoms of the adjacent pyridinecarboxamide units. Moreover, these units are buried in the hollow of the helix and so should not be available in any great number for hydrogen bonding unless partial unfolding occurs. However, the amide groups of the diacylaminopyridine units residing at the terminal positions of the oligomers are not buried in the helix hollow, and the most peripheral amidic protons are not involved in intramolecular hydrogen bonding. The terminal units should thus be available for hydrogen bonding with chiral carboxylic acids, possibly giving rise to chiral induction of helical handedness (Scheme 3).



Scheme 3. Expected hydrogen-bonding modes between carboxylic acids and the terminal acylaminopyridine units of **2**.

To test whether carboxylic acids bind to the terminal diacylaminopyridine units, heptamer **2** was titrated against (*S*)-phenylpropionic acid **3** and the experiment was monitored by ^{1}H NMR spectroscopy (Figure 4). The amidic protons of **2** give rise to four distinct signals. Six of these protons are strongly deshielded as a result of intramolecular hydrogen bonding and give three signals between 10 and 11 ppm. The two peripheral amides are not involved in hydrogen bonding and give one signal at 7.5 ppm. Upon addition of the acid, only two of these four signals shift downfield. The largest shift is recorded for the signal of the terminal amidic proton ($\Delta\delta$ = 0.4 ppm as opposed to $\Delta\delta$ = 0.15 ppm for the other proton). This is consistent with the formation of hydrogen bonds between the carboxylic acid and the peripheral acylaminopyridine units of **2**, as shown in Scheme 3. The chemical shift of one of the amide signals is unchanged during the titration and the fourth signal even undergoes an upfield shift which we have assigned to shielding effects of the phenyl group of the (*S*)-phenylpropionic acid bound to the terminal amide groups.

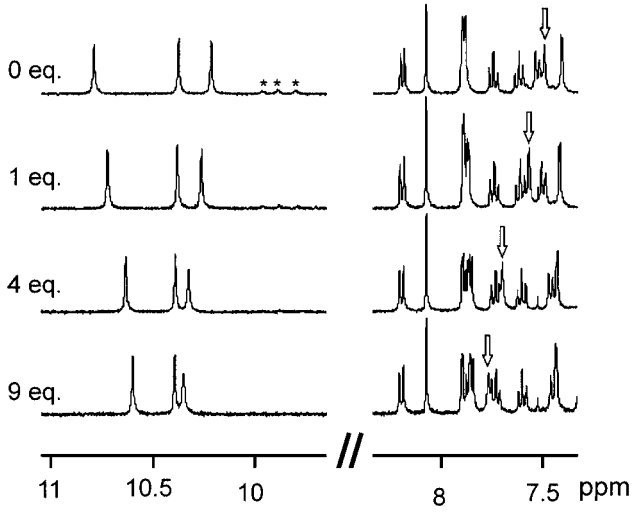


Figure 4. Part of the ^{1}H NMR (400 MHz) spectra of a 1 mM solution of **2** in $CDCl_3$ showing amide (10–11 ppm) and aromatic resonances (7–8.5 ppm) in the presence of increasing amounts of (*S*)-phenylpropionic acid. The arrows indicate the signal arising from the terminal amidic protons. The asterisks indicate the signals of trace amounts of the double helix of **2** that disappear upon addition of the acid (eq. = equivalents).

Note that a variation of 0.4 ppm in the chemical shift is smaller than expected for the formation of an acid–acylaminopyridine complex. Variations in chemical shifts as high as 2 ppm have been recorded in similar systems.[36] The small variation in the chemical shift observed for **2** is due to the fact that saturation is not reached at the low concentration of heptamer **2** used despite the excess of carboxylic acid added. The association constants between carboxylic acids and acylaminopyridines are low (typically less than 50 L mol^{-1}) and for oligomer **2**, this value is probably reduced by the presence of the neighboring pyridinedicarboxamide units. Thus only partial binding occurs under the conditions employed in the titration. Upon increasing the oligomer concentration, the titration is perturbed by the formation of double helices of **2**. Even in a 1 mM solution of **2**, a small amount of the double helical dimer can be detected in the NMR spectra (for this compound K_{dim} =

30 L mol^{-1} at 25 °C), which disappears upon addition of (*S*)-phenylpropionic acid (Figure 4). Addition of larger quantities of the acid seems to lead to partial unfolding of the strand (see below) possibly due to the bonding of acids to the central diacylaminopyridines or to a partial protonation of the pyridine rings.[26] Given the many equilibria involved, quantitative analysis of the titration data was not attempted.

That binding of chiral carboxylic acids to oligomer **2** results in the chiral induction of helical handedness was demonstrated by monitoring the titration experiments by CD spectroscopy. The titration of **2** against (*S*)-phenylpropionic acid (**3**) resulted in the appearance of two positive CD bands at 270 and 322 nm allied to the electronic transitions of the pyridine chromophores of heptamer **2** [see (a) in Figure 5]. These bands appear to be allied to the same chromophores as the bands observed in the spectra of chiral octamer **1** [see (a) in Figure 3]. The intensities of these bands reach a maximum when 10 equiv. of **3** are added. Upon addition of more acid, these intensities slowly decrease (not shown), which suggests that partial unfolding of the helices occurs. The maximum CD intensity reached with (*S*)-phenylpropionic acid (**3**) is about half that observed with chiral octamer **1** at the same temperature. This may result from a less efficient intermolecular chiral induction of handedness despite the fact that there are two sites of induction in the adduct **2**·**3**, whereas **1** has only one site of induction. The reduced intensity of the CD bands may also partly arise from the fact that hetpamer **2** is a little shorter than octamer **1**, which should result in a lower value of $\Delta\varepsilon$, and also from the fact that, under the conditions used, binding of phenylpropionic acid (**3**) to heptamer **2** does not reach saturation.

Interestingly, the bands induced by (*S*)-phenylpropionic acid (**3**) bound to heptamer **2** and the bands induced by the (*S*)-phenethylamino group of **1** all have the same sign. This indicates that the handedness induced intramolecularly in one case and intermolecularly in the other are identical. As shown in Figure 6, noncovalent binding of the (*R*)-phenylpropionic acid and covalent binding to the (*S*)-phenethylamino group may lead to comparable positioning of the proton, methyl and phenyl moieties at the asymmetric carbon atom. In the energy-minimized right-handed helices, the phenyl rings of the phenethylamino group and of phenylpropionic acid are both involved in the face-to-face aromatic stacking of the helix, whilst the methyl groups point away from the helix (Figure 6). These energy-minimized conformations compare well with the conformations observed in crystal structures of related quinoline-derived chiral oligomers.[29] These simple calculations thus suggest that the intra- and intermolecular inductions might occur by the same mechanism. However, further investigations will be required to demonstrate this point.

Chiral induction of helical handedness is also observed when **2** is titrated against (*R*)-mandelic acid (**4**) [see (b) in Figure 5]. The signs of the resulting CD bands are negative instead of positive as obtained with (*S*)-phenylpropionic acid (**3**). This suggests that chiral induction occurs in a similar manner in both compounds, and that the hydroxy group of **4** plays the same role as the methyl group of **3**. On the other hand, L-*N*-acetylphenylalanine (**5**) fails to induce any handedness [see (c) in Figure 5]. The titration with (*R*)-camphorsulfonic acid (**6**) results in chiral induction, however it is evident from the CD spectra that **2** behaves differently with **6** than it does with acids **3** and **4** on addition of increasing amounts of the acid [see (d) in Figure 5]. A more intense induced CD is observed after adding a single equivalent of **6**, and it reaches a maximum after the ad-

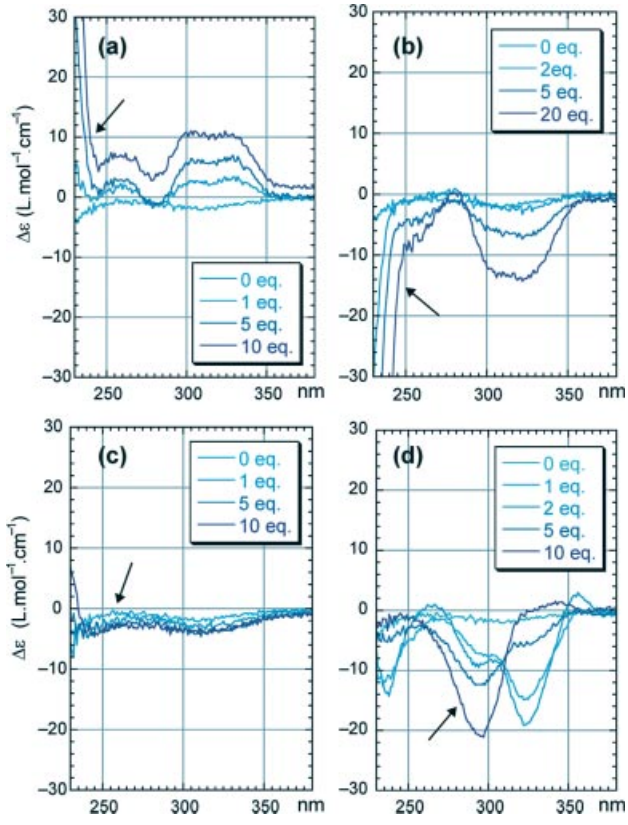


Figure 5. CD spectra of 1 mM solutions of heptamer **2** in $CHCl_3$ upon addition of increasing amounts of (a) (*S*)-phenylpropionic acid (**3**), (b) (*R*)-mandelic acid (**4**), (c) L-*N*-acetylphenylalanine (**5**), and (d) (*R*)-camphorsulfonic acid (**6**). The arrows indicate bands assigned to the four acids, the intensities of which increase as the concentration of added acid increases (eq. = equivalents).

Figure 6. Comparison of the energy-minimized models of the right-handed helical diastereoisomers of octameric strand (*R*)-**1**, which comprise a covalent bond to a (*R*)-phenethylamino group (left), and of a hydrogen-bonded complex between heptameric strand **2** and (*R*)-phenylpropionic acid (right). Alkoxy chains and benzyl carbamates were removed before energy minimization.

dition of 2 equivs. of **6**. The addition of further acid causes a rapid decrease and ultimately the disappearance of the induced band at 322 nm. This behavior results from the fact that the sulfonic acid **6** is considerably more acidic than carboxylic acids **3** and **4** and that it binds to heptamer **2** by a different mode. As we have shown previously,[26] sulfonic acids such as **6** in fact quantitatively protonate diacylaminopyridines in chloroform and lead to a conformational rearrangement of these units (Figure 7). The sulfonate anion interacts with the oligomeric strand through strong electrostatic interactions and hydrogen bonding to the amidic protons.[37–39] Heptamer **2** is expected to remain helical even after the protonation of both its terminal units, and chiral induction of helical handedness thus occurs in the presence of 2 equivs. or less of added (*R*)-camphorsulfonic acid (**6**). However, further protonation of the diaminopyridine units leads to the unfolding of the strand to an extended linear structure in which chiral induction is no longer possible.[26]

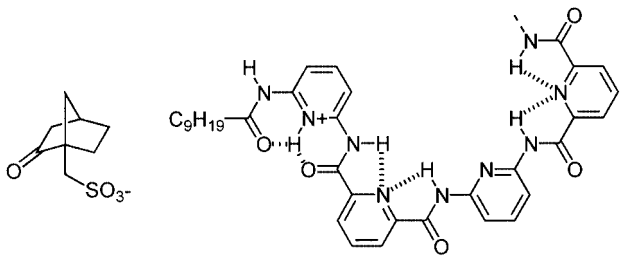


Figure 7. Rearrangement of the conformation of hetamer **2** upon protonation by acid **6**.

Intramolecular versus Intermolecular Chiral Induction

The results presented in the two previous sections suggest that intramolecular induction of helical handedness in **1** is more efficient than intermolecular induction in **2** even though two sites in heptamer **2** are likely to be involved in the intermolecular induction. We evaluated directly which of the two induction modes is the most efficient by titrating octamer (*S*)-**1** against chiral acids **3**–**6**. Octamer (*S*)-**1** possesses a chiral phenylethylamino group at one end which results in a bias of helical handedness leading to two positive CD bands. Octamer (*S*)-**1** also possesses a "free" diacylaminopyridine unit at the other end which should be available for binding to chiral acids. Titration of (*S*)-**1** against carboxylic acids **3**–**5** has no significant effect on its CD spectrum regardless of the configuration of the acid. This means that intramolecular induction of handedness prevails when intermolecular induction should act against it, and that no cooperativity occurs when both effects should operate simultaneously. Different behavior was observed upon titrating (*S*)-**1** against chiral sulfonic acids (*S*)- and (*R*)-**6** (Figure 8). Unexpectedly, after the addition of one equivalent of acid, the CD absorption of (*S*)-**1** at 322 nm was enhanced in both cases. This may simply be a result of a change in the chromophore from the pyridine to the pyridinium moiety. It may also be the result of a stronger intramolecular induction that occurs when the terminal diacylaminopyridine unit of **1** is protonated and adopts the conformation shown in Figure 7. The enhancement is slightly stronger with (*S*)-**6** than with (*R*)-**6**. This different behavior is consistent with cooperation between intra- and intermolecular chiral induction in one case and competition in the other. However, the effect is small, and the changes may as well be assigned to small differences in the relative orientation of the chromophores in the various diastereomeric complexes involved. Upon addition of further camphorsulfonic acid, the induced CD intensity decreases because of the unfolding of the helix that results from its progressive protonation (Figure 8). However, the decrease in the CD intensity occurs much faster with (*R*)-**6** than with (*S*)-**6**. Again, this is consistent with a positive cooperativity of intra- and intermolecular chiral induction in the case of (*S*)-**6** and a negative cooperativity in the case of (*R*)-**6**.

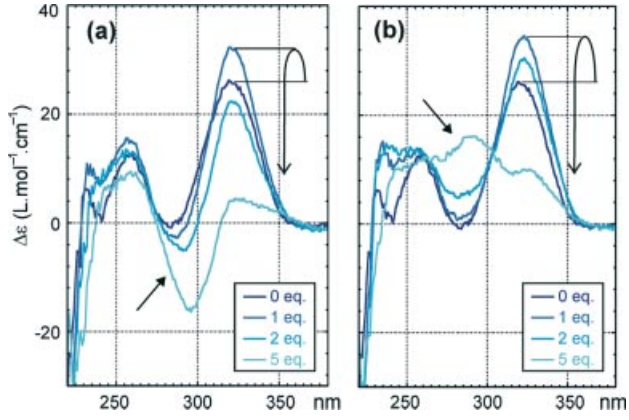


Figure 8. CD spectra of 1 mM solutions of octamer (*S*)-**1** in $CHCl_3$ upon addition of increasing amounts of (a) (*R*)-camphorsulfonic acid and (b) (*S*)-camphorsulfonic acid. The arrows indicate the bands assigned to the two acids (eq. = equivalents).

Conclusions

In summary, we have shown that both intramolecular and intermolecular chiral induction of handedness in helical oligoamides of 2,6-diaminopyridine and 2,6-pyridinedicarboxylic acid is possible. Intramolecular induction is effected by attaching a single chiral group to the end of an oligomer. Intermolecular induction results from various noncovalent interactions between chiral carboxylic or sulfonic acids and the terminal residues of the oligoamides. Intramolecular induction appears to be more efficient than intermolecular induction and prevails when both effects compete.

Several important aspects of these phenomena are still to be explored. First, the handedness of the induced conformation has not been assigned to a right- or left-handed helix, and this remains a particularly challenging task. Secondly, it might be possible to achieve intense chiral amplification and chiral memory effects by using longer oligomers or polymers for which inversion of helical handedness is

expected to be very slow. Finally, this paper has dealt only with the single helical conformations of the oligopyridinedicarboxamides. It will be interesting to see whether similar intra- and intermolecular induction of chiral handedness also occurs in their double helical conformations.

Experimental Section

General Remarks: Solvents (THF, toluene, and CH_2Cl_2) were dried by filtration through activated alumina on a commercially available setup. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded with a Bruker 400 Ultrashield spectrometer. Residual solvent peaks were used as internal standards. The following notation was used for the ^1H NMR splitting patterns: singlet (s), doublet (d), triplet (t), quintuplet (q), multiplet (m), and double doublet (dd). FTIR spectra were recorded with a Bruker FS 55 FT-IR spectrometer when using KBr pellets and with a Digilab TFS 2000 Scimitar instrument when using ATR. Melting points are uncorrected.

Benzyl (6-Aminopyridin-2-yl)carbamate (1b): At –78 °C, a 2.5 M solution of BuLi in hexane (132 mL, 330 mmol) was added to a solution of 2,6-diaminopyridine (10.9 g, 100 mmol) in anhydrous THF. After 1 h at this temperature the mixture was allowed to warm to room temp. for 1 h. The reaction mixture was then cooled to –78 °C and benzyl chloroformate (19 mL, 110 mmol) was added dropwise. The reaction mixture was then stirred at room temp. for 2 h before being cautiously quenched with water. The solvent was evaporated and the residue was dissolved in dichloromethane and washed with water. The organic layer was dried over $MgSO_4$, filtered, and the solvents evaporated. The residue was purified by flash chromatography on silica gel (eluent: CH_2Cl_2/EtOAc 95:5 v/v) to give the monoprotected amine **1b** as a white solid (20.3 g, yield 84%). M.p.: 60–65 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.2 (s, 2 H, NH_2), 5.10 (s, 2 H, OCH_2), 6.07 (d, ^3J(H,H) = 8.5 Hz, 1 H, C(3)-H), 7.17 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H, C(5)-H), 7.23–7.3 (m, 5 H, Aryl-H), 7.33 (dd, t, $^3J^1_{H,H} = {}^3J^2_{H,H}$ = 8.5 Hz, 1 H, C(4)-H), 7.54 ppm (s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.9, 101.7, 103.3, 128.1, 128.2, 128.4, 135.9, 139.9, 150.1, 152.9, 157.3 ppm. IR (KBr): $\tilde{\nu}$ = 3438, 3374, 3323, 3196, 1740, 1706, 1630, 1609, 1577, 1528, 1457, 1419, 1294, 1195, 1167, 1085, 1043, 905, 870, 846 cm^{-1}. EIMS: *m*/*z* = 243.30 $[M]^+$ (calcd. for $C_{13}H_{13}N_3O_2$: 243.10).

General Procedure for the Coupling Reaction (compounds 2a, 4a, and 8a): The starting acid (**1a**, **2c**, or **4c**) was converted to its corresponding acid chloride in refluxing $SOCl_2$ (50 equiv.). The reaction was stopped when no more gas formation was observed. The remaining $SOCl_2$ was distilled off and the resulting solid was dried in vacuo and then dissolved in anhydrous toluene or CH_2Cl_2 before 2 equiv. of diisopropylethylamine were added. Amine **1b**, **2b**, or **4b** (1 equiv.) was added to this solution. The reaction mixture was stirred at room temp. for 12 h and then quenched with water. The solution was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered, and the solvents evaporated. The resulting solid was purified by flash chromatography on silica gel.

Dimer Carbamate Ester 2a: As described in the general coupling procedure, monoacid-monoester **1a** (3.85 g, 11.42 mmol) and monoamine **1b** (2.78 g, 11.42 mmol) were coupled to give dimer **2a** as a white powder (6.54 g, yield 98%). M.p.: 138–140 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{H,H}$ = 7 Hz, 3 H, C-CH_3), 1.2–1.4 (m, 14 H), 1.47 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 1.84 (q, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 4.02 (s, 3 H, O-CH_3), 4.15 (t, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 5.22 (s, 2 H, OCH_2Ph), 7.33–7.42 (m, 5 H, C_{aryl}-H), 7.46 (s, 1 H, NH), 7.72–7.80 (m, 3 H, C_{aryl}-H), 7.91 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, C_{aryl}-H), 8.04 (dd, $^4J^1_{H,H}$ = 2.5, $^3J^2_{H,H}$ = 6 Hz, 1 H, C_{aryl}-H), 10.27 ppm (s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.5 (CH_3), 23.0 (CH_2), 26.2 (CH_2), 29.1 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 32.2 (CH_2), 53.6 (OCH_3), 67.5 (OCH_2), 69.6 (OCH_2), 108.9 (CH_{aryl}), 109.8 (CH_{aryl}), 112.4 (CH_{aryl}), 114.9 (CH_{aryl}), 128.4 (CH_{aryl}), 128.6 (CH_{aryl}), 128.8 (CH_{aryl}), 135.9 ($C_{quat.}$), 141.0 ($C_{quat.}$), 149.4 ($C_{quat.}$), 150.6 ($C_{quat.}$), 150.8 ($C_{quat.}$), 153.5 ($C_{quat.}$), 162.0 ($C_{quat.}$), 168.3 ppm ($C_{quat.}$). IR (ATR): $\tilde{\nu}$ = 3358, 2923, 2852, 2360, 2341, 1739, 1712, 1698, 1586, 1533, 1508, 1452, 1344, 1293, 1253, 1156, 1109, 1088, 1031, 902, 875, 846, 806, 788, 762, 733, 694 cm^{-1}. MALDI-TOF MS: *m*/*z* = 563.20 $[M + H]^+$ (calcd. for $C_{31}H_{39}N_4O_6$: 563.29).

Tetramer Carbamate Ester 4a: As described in the general coupling procedure, dimer acid **2c** (1.95 g, 3.55 mmol) and dimer amine **2b** (1.5 g, 3.55 mmol) were coupled to give tetramer **4a** as a white powder (3 g, yield 89%). M.p. 134–136 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{H,H}$ = 7 Hz, 6 H, CH_2CH_3), 1.2–1.4 (m, 28 H), 1.48 (q, $^3J_{H,H}$ = 7 Hz, 4 H), 1.85 (m, 4 H, OCH_2CH_2), 3.79 (s, 3 H, OCH_3), 4.06 (t, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 4.19 (t, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 5.01 (s, 2 H, OCH_2Ph), 7.03–7.17 (m, 5 H, $C_{aryl}H$), 7.47 (d, $^4J_{H,H}$ = 2 Hz, 1 H, $C_{aryl}H$), 7.70 (dd, $^3J^1_{H,H} = {}^3J^2_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 7.74 (dd, $^3J^1_{H,H} = {}^3J^2_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 7.81 (d, $^3J_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 7.84 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 7.91 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 7.93 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 8.01 (d, $^3J_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 8.10 (d, $^3J_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 8.14 (s, 1 H, NH), 8.15 (d, $^3J_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 10.55 (s, 1 H, NH), 10.62 (s, 1 H, NH), 10.69 ppm (s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.60, 23.19, 26.37, 26.41, 29.34, 29.36, 29.42, 29.84, 29.85, 29.88, 29.90, 30.08, 30.10, 30.15, 53.24, 67.03, 69.58, 69.66, 69.77, 108.16, 108.73, 110.18, 110.54, 110.94, 111.78, 112.05, 127.69, 128.21, 128.65, 148.85, 149.45, 149.82, 150.35, 150.58, 152.74, 161.68, 164.66, 167.53, 168.21, 115.28, 161.29, 151.72 ppm. IR (ATR): $\tilde{\nu}$ = 3284, 2924, 2854, 1733, 1692, 1585, 1504, 1450, 1394, 1343, 1292, 1243, 1212, 1157, 1111, 1087, 1037, 1003, 880, 840, 798, 767, 733, 695 cm^{-1}. MALDI-TOF MS: *m*/*z* = 959.50 $[M + H]^+$ (calcd. for $C_{53}H_{67}N_8O_9$: 959.50).

Octamer Carbamate Ester 8a: According to the general coupling procedure, tetramer acid **4c** (700 mg, 0.753 mmol) and tetramer amine **4b** (610 mg, 0.753 mmol) were coupled to give octamer **8a** (720 mg, yield 55%). M.p.: 205–207 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (m, 12 H, CH_2CH_3), 1.23–1.50 (m, 56 H), 1.56 (q, $^3J_{H,H}$ = 7.3 Hz, 8 H), 1.92 (q, $^3J_{H,H}$ = 7.4 Hz, 8 H, OCH_2CH_2), 3.58 (s, 3 H, OCH_3), 3.97–4.31 (m, 8 H, OCH_2CH_2), 4.84 (m, 1 H, OCH_2Ph), 5.23 (m, 1 H, OCH_2Ph), 6.99–7.12 (m, 5 H), 7.27–7.37 (m, 4 H), 7.53–7.76 (m, 4 H), 7.79 (s, 1 H, NH), 7.80–7.91 (m, 4 H), 7.89 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, $C_{aryl}H$), 8.17 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, $C_{aryl}H$), 10.32 (s, 1 H, NH), 10.41 (s, 1 H, NH), 10.43 (s, 1 H, NH), 10.45 (s, 1 H, NH), 10.52 (s, 1 H, NH), 10.54 (s, 1 H, NH), 10.81 ppm (s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.8, 26.0, 26.1, 29.0, 29.5, 29.7, 32.0, 52.8, 66.9, 69.2, 69.4, 107.8, 108.4, 109.7, 109.9, 110.1, 110.9, 111.2, 111.3, 111.4, 111.5, 112.1, 115.2, 127.1, 127.6, 128.2, 135.8, 140.8, 141.0, 141.4, 146.1, 148.5, 148.6, 148.7, 148.9, 149.1, 149.2, 149.3, 149.9, 150.1, 151.6, 152.1, 160.3, 160.4, 161.1, 161.2, 161.6, 164.0, 167.2, 167.6, 167.9, 168.0 ppm. IR (KBr): $\tilde{\nu}$ = 2925, 2854, 1736, 1699, 1587, 1522, 1458, 1392, 1376, 1345, 1299, 1246, 1213, 1158, 1115, 1086, 1038, 998, 879, 800, 730, 693 cm^{-1}. ESMS: *m*/*z* = 1752.20 $[M + H]^+$ (calcd. for $C_{97}H_{124}N_{16}O_{15}$: 1752.94), 876.60 $[M + 2H]^{2+}$ (calcd. for $C_{97}H_{125}N_{16}O_{15}$: 876.97).

General Procedure for the Saponification of the Methyl Esters (Preparation of 2c, 4c, and 8c): Ester **2a**, **4a**, or **8a** was dissolved in a mixture of dioxane/H_2O (8:2 v/v) in the presence of KOH (4 equiv.). The reaction was monitored by TLC and stirred at room temp. until no starting material could be detected. The reaction mixture was then neutralized with acetic acid and the dioxane was evaporated. The resulting white solid was filtered, washed with water, and dried under vacuum. It was used in the next step without further purification. Its purity was checked only by ^{1}H NMR and mass spectrometry.

Dimer Carbamate Acid 2c: Saponification of dimer **2a** (2 g, 3.56 mmol) as described in the general procedure, gave acid **2c** as a white solid (1.95 g, yield 98%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.85 (t, $^3J_{H,H}$ = 7 Hz, 3 H, CH_2CH_3), 1.16–1.37 (m, 14 H), 1.42 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 1.78 (q, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 4.26 (t, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 5.19 (s, 2 H, OCH_2Ph), 7.30–7.46 (m, 5 H, $C_{aryl}H$), 7.65 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 1.0 Hz, 1 H, $C_{aryl}H$), 7.75 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 7.84 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 7.85–7.95 (m, 2 H, $C_{aryl}H$), 10.36 (s, 1 H, NH), 10.53 ppm (s, 1 H, NH). MALDI-TOF MS: *m*/*z* = 549.20 [M + H]$^+$ (calcd. for $C_{30}H_{37}N_4O_6$: 549.27).

Tetramer Carbamate Acid 4c: Tetramer **4a** (720 mg, 3.56 mmol) was saponified, as described in the general saponification procedure, to give acid **4c** as a white powder (700 mg, yield 98%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.04 (t, $^3J_{H,H}$ = 6.5 Hz, 6 H, CH_2CH_3), 0.38–0.58 (m, 28 H), 0.65 (m, 4 H), 1.01 (m, 4 H, OCH_2CH_2), 3.31 (t, $^3J_{H,H}$ = 6.2 Hz, 2 H, OCH_2CH_2), 3.40 (t, $^3J_{H,H}$ = 6.1 Hz, 2 H, OCH_2CH_2), 4.26 (s, 2 H, OCH_2Ph), 6.37 (m, 5 H), 6.85 (d, $^4J_{H,H}$ = 2.2 Hz, 1 H, $C_{aryl}H$), 6.87 (d, $^3J_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 6.96 (dd, $^3J^1_{H,H}$ = $^3J^2_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 6.95 (dd, $^3J^1_{H,H}$ = $^3J^2_{H,H}$ = 8 Hz, 1 H, $C_{aryl}H$), 7.00–7.12 (m, 5 H, $C_{aryl}H$), 7.16 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, $C_{aryl}H$), 7.33 (dd, $^3J^1_{H,H}$ = $^3J^2_{H,H}$ = 7.8 Hz, 1 H, $C_{aryl}H$), 8.56 (s, 1 H, NH), 10.27 (s, 1 H, NH), 10.28 (s, 1 H, NH), 10.43 ppm (s, 1 H, NH). MALDI-TOF MS: *m*/*z* = 945.50 [M + H]$^+$ (calcd. for $C_{52}H_{65}N_8O_9$: 945.49).

Octamer Carbamate Acid 8c: Acid **8c** was obtained as a white powder by saponification of the octamer **8a** (200 mg, 0.114 mmol) following the general procedure (190 mg, yield 98%). NMR spectra showed broad signals in all the solvents tested. MALDI-TOF MS: *m*/*z* = 1737.69 [M + H]$^+$ (calcd. for $C_{96}H_{121}N_{16}O_{15}$: 1737.92), 1759.66 [M + Na]$^+$ (calcd. for $C_{97}H_{120}N_{16}NaO_{15}$: 1759.90).

General Procedure for the Hydrogenolysis of Benzyl Carbamate Protecting Groups (Synthesis of 2b and 4b): The protected amine **2a** or **4a** and 10% palladium on activated carbon (10%, wt/wt) were mixed in a mixture of DMF/methanol (8:2, v/v). The mixture was placed under hydrogen and stirred until no starting compound could be observed by TLC. The suspension was then diluted with CH_2Cl_2 and filtered through a Celite pad to remove the catalyst. The filtrate was evaporated to give the free amine. The amine was used without further purification, but was rigorously dried by using a Dean–Stark apparatus and by running a continuous distillation in toluene at atmospheric pressure before performing subsequent coupling reactions. The purity of the amine was simply checked by NMR and mass spectrometry.

Dimer Ester Amine 2b: Hydrogenation, following the general procedure described above, of dimer **2a** (2 g, 3.56 mmol) for 2 h leads to the formation of amine **2b** as a white powder (1.5 g, yield 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{H,H}$ = 7 Hz, 3 H, CH_2CH_3), 1.2–1.4 (m, 14 H), 1.47 (q, $^3J_{H,H}$ = 7 Hz, 2 H), 1.84 (q, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 4.03 (s, 3 H, OCH_3), 4.15 (t, $^3J_{H,H}$ = 7 Hz, 2 H, OCH_2CH_2), 4.41 (s, 2 H, NH_2), 6.31 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, $C_{aryl}H$), 7,52 (t, $^3J_{H,H}$ = 7.8 Hz, 1 H, $C_{aryl}H$), 7.72 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, $C_{aryl}H$), 7.74 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 7.93 (d, $^4J_{H,H}$ = 2.5 Hz, 1 H, $C_{aryl}H$), 10.20 ppm (s, 1 H, NH). MALDI-TOF MS: *m*/*z* = 429.20 [M + H]$^+$ (calcd. for $C_{23}H_{33}N_4O_4$: 429.25).

Tetramer Ester Amine 4b: Tetramer amine **4b** was obtained as a white powder from tetramer **4a** (720 mg, 0.76 mmol) according to the general hydrogenation procedure (610 mg, yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, $^3J_{H,H}$ = 6.4 Hz, 6 H, CH_2CH_3), 1.2–1.4 (m, 28 H), 1.48 (q, $^3J_{H,H}$ = 6.4 Hz, 4 H), 1.85 (m, 4 H, OCH_2CH_2), 3.96 (s, 3 H, OCH_3), 4.16 (t, $^3J_{H,H}$ = 6.7 Hz, 2 H, OCH_2CH_2), 4.19 (t, $^3J_{H,H}$ = 6.7 Hz, 2 H, OCH_2CH_2), 4.68 (s, 2 H, NH_2), 6.31 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, $C_{aryl}H$), 7.56 (t, $^3J_{H,H}$ = 7.9 Hz, 1 H, $C_{aryl}H$), 7.75 (d, $^4J_{H,H}$ = 2.6 Hz, 1 H, $C_{aryl}H$), 7.78 (d, $^3J_{H,H}$ = 8.2 Hz, 1 H, $C_{aryl}H$), 7.87 (dd, $^3J^1_{H,H}$ = $^3J^2_{H,H}$ = 8.2 Hz, 1 H, $C_{aryl}H$), 7.94 (d, $^4J_{H,H}$ = 2.6 Hz, 1 H, $C_{aryl}H$), 7.98 (d, $^4J_{H,H}$ = 2.6 Hz, 1 H, $C_{aryl}H$), 7.99 (d, $^4J_{H,H}$ = 2.6 Hz, 1 H, $C_{aryl}H$), 8.14 (dd, $^3J_{H,H}$ = 8.2, $^4J_{H,H}$ = 0.6 Hz, 1 H, $C_{aryl}H$), 8.26 (dd, $^3J_{H,H}$ = 8.2, $^4J_{H,H}$ = 0.6 Hz, 1 H, $C_{aryl}H$), 10.26 (s, 1 H, NH), 10.44 ppm (s, 2 H, NH). MALDI-TOF MS: *m*/*z* = 825.50 [M + H]$^+$ (calcd. for $C_{45}H_{61}N_8O_7$: 825.47).

Chiral Octamer Carbamate Amides (*S*)-1 and (*R*)-1: Octamer acid **8c** (8 mg, 4,6 μmol) was dissolved in anhydrous DMF (2 mL) before diisopropylethylamine (50 μL) was added followed by HBTU (2 mg, 5.2 μmol). The mixture was stirred at ambient temperature for 10 min. (*R*)- or (*S*)-α-methylbenzylamine (0.6 μL, 5 μmol) was added and the mixture was stirred for 2 h. The solvent was evaporated in vacuo and the residue was purified by silica gel chromatography to give chiral octamer (*R*)-**1** or (*S*)-**1** as a white solid. M.p.: 180–183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78–0.96 (m), 1.05–1.63 (m), 1.80–2.03 (m), 4.0–4.33 (m, 8 H, OCH_2CH_2), 4.78–4.87 (m, 2 H, OCH_2Ph and $NHCHPh$), 5.13 (m, 1 H, OCH_2Ph), 6.94–7.16 (m), 7.20 (d, $^4J_{H,H}$ = 1.9 Hz, 1 H, $C_{aryl}H$), 7.33 (s), 7.40 (d, $^4J_{H,H}$ = 1.9 Hz, 1 H, $C_{aryl}H$), 7.58–7.74 (m), 7.75–7.81 (m), 7.88 (d, $^4J_{H,H}$ = 2.4 Hz, 1 H, $C_{aryl}H$), 7.88–7.98 (m), 8.07–8.15 (m), 8.26

Table 1. Crystallographic data for compound **2a**.

Compound	**2a**
Formula	$C_{31}H_{38}N_4O_6$
Mol. mass [g mol^{-1}]	562.66
Crystal system	monoclinic
Space group	$P\bar{1}$
a [Å]	8.131(1)
b [Å]	10.991(2)
c [Å]	18.612(2)
α [°]	74.70(1)
β [°]	81.13(1)
γ [°]	68.55(1)
V [Å^3]	1490.2(4)
$D_{calcd.}$ [g cm^{-3}]	1.254
Z	2
F[000]	600
μ (Cu-K_α) [mm^{-1}]	0.715
Crystal color	Colorless
Crystal size [mm]	0.5 × 0.25 × 0.15
Data collection	
θ_{min}, θ_{max} [°]	4.44, 65.12
Temperature [K]	296(2)
Reflections collected	5080
Reflections unique	5080
Refinement	
No. of parameters	377
$R1$ [$I > 2\sigma(I)$]	0.0462
wR_2 (all data)	0.1354
GOF	1.041

(m, 1 H), 10.10 (s, 1 H, NH), 10.32 (s, 1 H, NH), 10.39 (s, 1 H, NH), 10.47 (br. s, 2 H, NH), 10.66 ppm (s, 2 H, NH). The ^{13}C NMR spectrum is broad and very complex. At the high concentration used for acquisition, it contains signals belonging to multiple species such as the right- and left-handed single helices, and various right- and left-handed double helices with parallel or antiparallel arrangements of the strands. IR (KBr): $\tilde{\nu}$ = 2959, 2924, 2854, 2346, 1871, 1862, 1831, 1813, 1803, 1794, 1774, 1763, 1741, 1736, 1701, 1691, 1686, 1665, 1655, 1648, 1637, 1587, 1571, 1560, 1523, 1459, 1348, 1262, 1092, 1044, 801 cm^{-1}. MALDI-TOF MS: *m*/*z* = 1841.93 $[M + H]^+$ (calcd. for $C_{104}H_{130}N_{17}O_{14}$: 1842.25), 1864.03 $[M + Na]^+$ (calcd. for $C_{104}H_{130}N_{16}NaO_{15}$: 1864.23).

X-ray Crystallographic Study: The structure of **2a** was determined by single-crystal X-ray diffraction analysis. The data were collected on a CAD4 Enraf–Nonius diffractometer with graphite-monochromatized Cu-K_α radiation. The cell parameters were determined by least-squares from the setting angles of 25 reflections. An empirical absorption correction was applied. The data were also corrected for Lorentzian and polarization effects. The crystals are mechanically fragile as well as unstable in air. During exposure to X-rays, the crystals and some of the mother liquor were sealed in a Lindemann glass capillary. The positions of non-hydrogen atoms were determined by the SHELXS-97 program[40] and the position of the hydrogen atoms were deduced from coordinates of the non-hydrogen atoms and confirmed by Fourier synthesis. Hydrogen atoms were included for structure factor calculations but were not refined. CCDC-249796 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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