Sterically controlled naphthalene homo-oligoamides with novel structural architectures†

Panchami Prabhakaran,[a] Vedavati G. Puranik,[b] Jima N. Chandran,[c] P. R. Rajamohanan,*[c] Hans-Jörg Hofmann*[d] and Gangadhar J. Sanjayan*[a]

Received 9th December 2008, Accepted 16th February 2009
First published as an Advance Article on the web 19th March 2009
DOI: 10.1039/b822076j

Herein we report novel naphthalene homo-oligoamides, derived from 4-amino-3-methoxy-naphthalene-2-carboxylic acid and 4-amino-1-methoxy-naphthalene-2-carboxylic acid as monomer building blocks, that display an anti-periplanar arrangement of the naphthyl rings, primarily induced by steric interactions between adjacent groups and functionalities.

Introduction

In the last three decades, considerable efforts in the generation of biotic and abiotic synthetic oligomers have led to the development of a wide variety of backbone architectures exhibiting novel features and functions.[1–4] Among the abiotic oligomers, aromatic foldamers have attracted special attention because of the relative ease of synthesis and prediction of the conformation and their high structural stability.[4] The majority of aromatic oligomers are with oligoamide backbones having an amino group in the *meta* position to a carboxylic group appended on the aryl ring. This gives an inherent driving force to bend the backbone, such that shorter oligomers generally adopt a planar crescent conformation while their larger counterparts adopt well-defined helical conformations.[5] For attaining a stable conformation, the rotations about the Ar–CO and Ar–NH bonds have to be restricted, which is mostly achieved by S(6) or S(5) hydrogen bonding between the side chains and the backbone, within the backbone, or between side chains.[4,6,7] Hydrogen bonding has been of considerable utility in structural pre-organization owing to its directionality and specificity,[8] but other secondary interactions such as metal coordination are also found to be suited for the design of conformationally ordered systems.[9]

In contrast, synthetic oligomers with structural pre-organization primarily effected by steric interactions are relatively rare in the literature, although the importance of steric interactions for structure formation is not less than that of hydrogen bonding.[10] Herein, we describe the design, synthesis, and conformational analysis of naphthalene homo-oligoamides whose conformational pre-organization is mainly effected by steric interactions. These aromatic homo-oligoamides are derived from 4-amino-3-methoxy-naphthalene-2-carboxylic acid and 4-amino-1-methoxy-naphthalene-2-carboxylic acid building blocks. The conformational investigations suggest that these oligomers display an anti-periplanar arrangement of the naphthyl rings, a conformational feature that is in strong contrast to the corresponding oligobenzamides.[11]

Design strategy

In order to exploit the steric interactions in conformational ordering, we designed building blocks containing naphthyl units (Fig. 1). It was anticipated that the steric hindrance in the dimer building blocks could lead to restricted rotation, which would force the naphthyl rings to adopt an anti-periplanar conformations, as depicted in Fig. 1c,d. Such an arrangement would also deprive the naphthyl building block of the possibility of bifurcated hydrogen

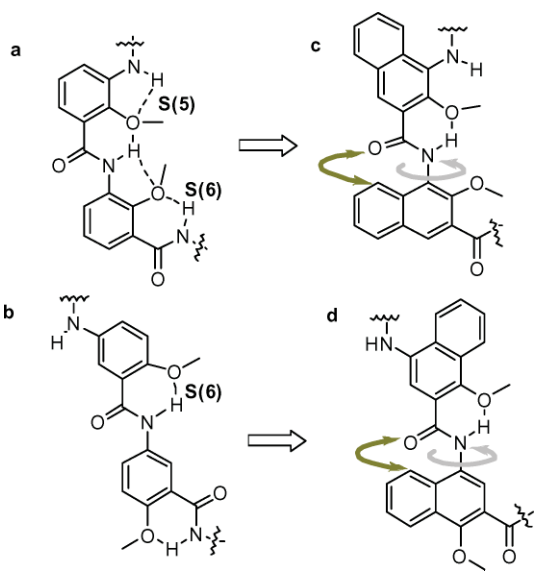


Fig. 1 Illustration of the design strategy which takes profit from steric interactions to get non-planar aryl conformations in structures **c** and **d** (indicated by curved double-headed olive-green arrows). For comparison, the corresponding oligobenzamides are given (structures **a** and **b**).

[a]*Division of Organic Chemistry, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, 411 008, India. E-mail: gj.sanjayan@ncl.res.in; Fax: (+91) 020-25893153; Tel: (+91) 020-25902082*
[b]*Central Material Characterization Division, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, 411 008, India*
[c]*Central NMR Facility, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune, 411 008, India. Fax: (+91) 020-25893153; Tel: (+91) 020-25902075*
[d]*Universität Leipzig, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Institut für Biochemie, Brüderstraße 34, D-04103, Leipzig, Germany. E-mail: hofmann@rz.uni-leipzig.de*

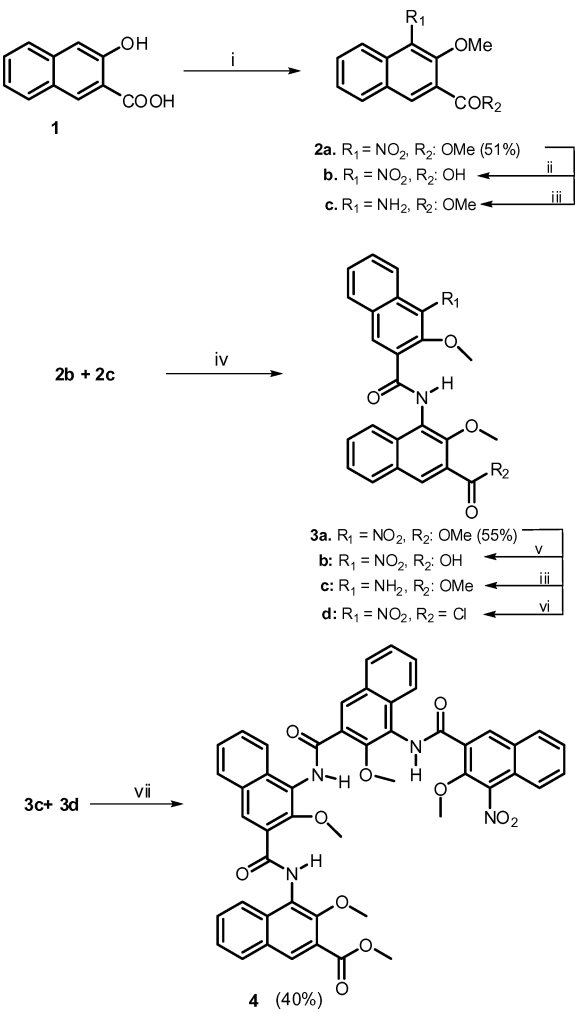
† Electronic supplementary information (ESI) available: ^{1}H, ^{13}C, and DEPT-135 NMR spectra, ESI mass spectra and 2D spectra of compounds, details of *ab initio* MO calculations, HF/6-31G* structures of **4** and **8**; crystal data for **3a** and **7b** in CIF format.[20] See DOI: 10.1039/b822076j

bonding involving adjacent residues, as seen in the corresponding oligobenzamides (Fig. 1a). The oligomers derived from such building blocks were expected to possess the S(6)-type of intramolecular hydrogen bonding interaction, which would further support the conformational ordering.[12] Furthermore, the conformational features could be considerably influenced by the positioning of the hydrogen bond-directing alkoxy oxygens as hydrogen bond acceptors, appended on the periphery of the naphthyl rings.

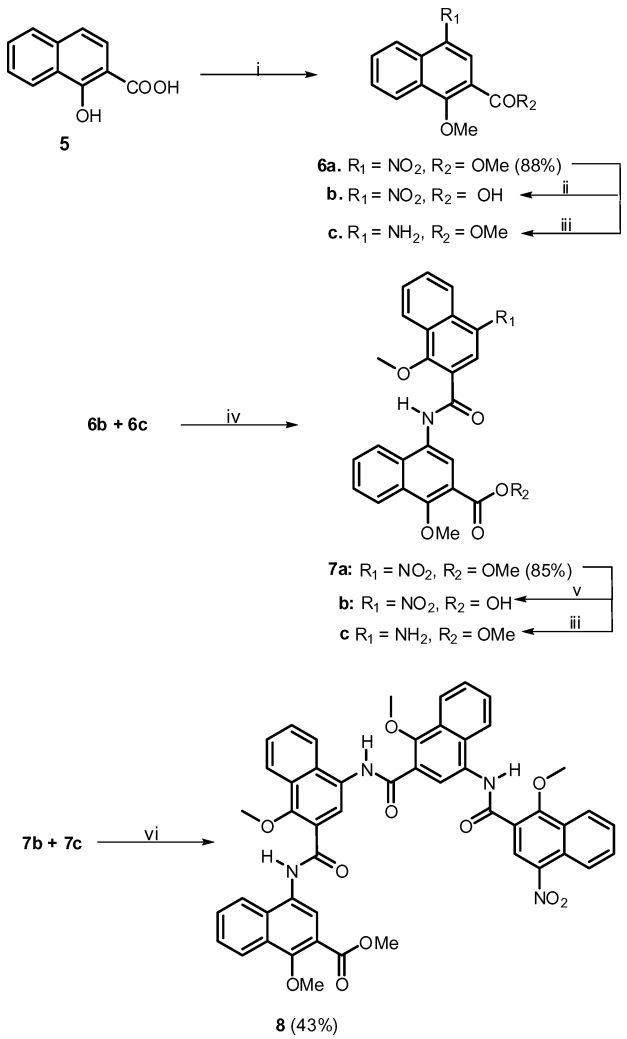
Results and discussion

Synthesis

The building blocks **2a** and **6a**, required for the oligomer synthesis, were accessed from 3-hydroxy-2-naphthoic acid **1** (Scheme 1) and 1-hydroxy-2-naphthoic acid **5** (Scheme 2), respectively. Esterification of **1** followed by careful nitration and subsequent *O*-methylation furnished the building block **2a** in 51% overall yield. The acid **2b**, obtained by saponification of **2a**, was coupled with the amine **2c** using DCC as the coupling agent to obtain the



Scheme 1 *Reagents and conditions:* (i) (a) MeOH, H_2SO_4 (cat.), reflux, 12 h; (b) Conc. HNO_3, conc. H_2SO_4 (cat.), DCM, 0 °C, 10–15 min; (c) dimethyl sulfate, K_2CO_3, acetone, 12 h, rt. (ii) LiOH, MeOH, 12 h, rt; (iii) Pd/C, H_2, AcOEt, 6 h; (iv) DCC, DCM, 12 h; (v) LiOH, dioxane, rt, 12 h; (vi) $(COCl)_2$, DMF (cat.), DCM, rt, 3 h; (vii) Et_3N, rt, 12 h.



Scheme 2 *Reagents and conditions:* (i) (a) dimethyl sulfate, K_2CO_3, acetone, 12 h, rt; (b) Conc. HNO_3, conc. H_2SO_4 (cat.), DCM, 0 °C, 10–15 min; (ii) LiOH, MeOH, 12 h; (iii) Pd/C, H_2, AcOEt, 6 h; (iv) HBTU, MeCN, DIEA, rt, 12 h; (v) LiOH, dioxane, rt, 12 h; (vi) HBTU, MeCN, DIEA, 60 °C, 12 h.

dimer **3a** in 55% yield (Scheme 1). The higher-order oligomer **4** was obtained from the dimer **3a** following a 'segment doubling strategy'.[13]

The building block methyl-1-methoxy-4-nitro-2-naphthoate **6a**, required for the construction of oligomers **7** and **8**, was accessed starting from 1-hydroxy-2-naphthoic acid **5** (Scheme 2). Simultaneous esterification and *O*-methylation of **5** using dimethyl sulfate followed by controlled nitration with conc. HNO_3 afforded **6a** in 88% yield. The oligomers **7** and **8** were obtained from **6** following segment doubling strategy, involving HBTU as the coupling agent.

Single-crystal X-ray diffraction studies

Single crystals of the dimer **3a** suitable for X-ray diffraction studies were obtained by crystallization from a mixture of ethyl acetate and pet. ether. Analysis of the crystal structure[14] reveals that the two naphthyl rings, joined by an amide bond, do not lie in the same plane due to steric hindrance (Fig. 2a), as anticipated. They are rotated by about 49° and 72° respectively with respect to the amide

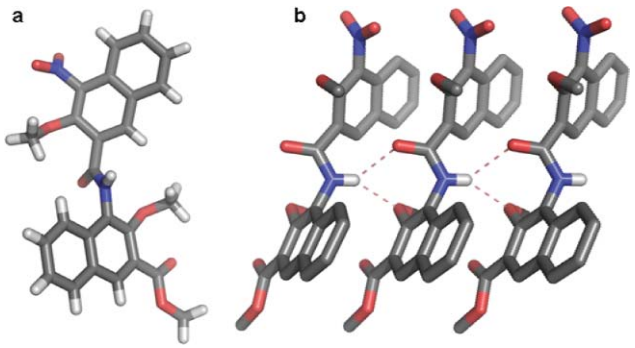


Fig. 2 (a) Crystal structure of dimer **3a**; (b) one-dimensional packing effected by dispersion interactions (π–π stacking) and bifurcated hydrogen bonding.

plane, adopting an approximate anti-periplanar conformation and causing the amide group to be solvent-exposed. This enables the molecules to undergo aggregation in the crystal package *via* dispersion interactions (π–π stacking)[15] and bifurcated intermolecular hydrogen bonding interaction (Fig. 2b). Due to these packing effects, the expected intramolecular S(6)-type hydrogen bonding is missing in the crystal structure.[16] Nevertheless, the sterically driven non-planar arrangement of the naphthyl rings is clearly evident.

In the solid-state conformation of dimer amine **7c**, the two naphthyl rings are almost perpendicular to each other due to the steric interactions, as expected (Fig. 3). The molecule retains the anticipated S(6)-type intramolecular N–H $\cdots$ O hydrogen bonding between the amide NH and OMe of the adjacent aryl ring [d(N $\cdots$ O) = 2.736(7) Å and d(H $\cdots$ O) = 2.07 Å, and the bond angle (N–H $\cdots$ O) = 134°].

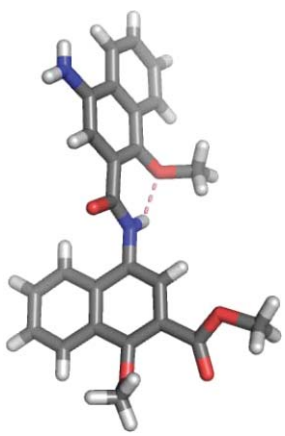


Fig. 3 Crystal structure of **7c** displaying a non-planar arrangement of the naphthyl rings with S(6)-type intramolecular N–H $\cdots$ O hydrogen bonding.

NMR studies

A detailed NMR study was performed to investigate the solution-state conformation of the oligomers (400/500 MHz, $CDCl_3$). In order to study the hydrogen-bonding interactions in the solution state (intra- *vs* intermolecular), solvent dilution ($CDCl_3$) and titration (DMSO-d_6) experiments were carried out (see ESI†). Solvent titration/dilution experiments provide convincing evidence for distinguishing intramolecular from intermolecular hydrogen bonding interactions.[3h,17] Whereas solvent-exposed amide NHs are considerably shifted in titration/dilution experiments, solvent-shielded (solvent-masked) NHs undergo negligible shifts with varying concentration or polarity of the solvent since they are inaccessible to solvent effects. The negligible shifts observed in dilution and titration experiments on the oligomers [**3a**: ($\Delta\delta(NH)_{titration} < 0.16$ ppm, $\Delta\delta(NH)_{dilution} < 0.02$ ppm), **4**: ($\Delta\delta(NH1)_{titration} < 0.34$ ppm, $\Delta\delta(NH2)_{titration}$, $\Delta\delta(NH3)_{titration} < 0.14$ ppm), **7a**: ($\Delta\delta(NH)_{titration} < 0.09$ ppm, $\Delta\delta(NH)_{dilution} < 0.03$ ppm) and **8**: ($\Delta\delta(NH1)_{titration} < 0.24$ ppm, $\Delta\delta(NH2)_{titration} < 0.14$ ppm, $\Delta\delta(NH3)_{titration} < 0.07$ ppm) suggest that all amide NHs are involved in strong intramolecular hydrogen bonding interactions (Fig. S1–S6†).

2D NOESY studies provided insight into the solution-state conformation of these oligomers. The signals were assigned unambiguously based on 2D COSY, HSQC, TOCSY, HMBC, and NOESY experiments. The spectra and signal assignments are provided in the ESI†.

In the dimer **3a**, the amide NH displayed a stronger dipolar coupling with OMe1 when compared to OMe2 (Fig. 4a). This is surprising given the fact that OMe2 and NH are closer in the crystal structure as indicated by the distances d(NH–OMe1) = 3.34 Å and d(NH–OMe2) = 2.99 Å, respectively. The relatively stronger NOE between the amide NH and OMe1 suggests that S(6)-type intramolecular hydrogen bonding is clearly prevalent in solution, as already substantiated by the solvent dilution/titration experiments (Fig. S1–S6†).

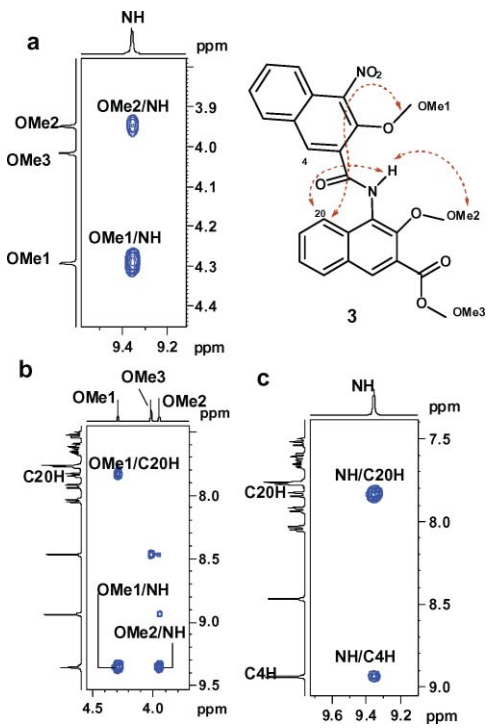


Fig. 4 2D extracts of **3a** (500 MHz, $CDCl_3$). (a) NH *vs* OMe; (b) OMe *vs* ArH; (c) NH *vs* ArH.

Although a shorter distance of d(OMe2–C4H) = 2.6 Å was observed between OMe2 and C4H in the crystal structure, inspection of the 2D data reveals a weak NOE between OMe2 and C4H. According to the solid-state conformation, NH is expected to show dipolar coupling with C20H and C4H with

distances of d(NH–C4H) = 2.4 Å and d(NH–C20H) = 2.6 Å, respectively. However, inspection of 2D NOESY data revealed a stronger dipolar coupling of NH with C20H in comparison with C4H (Fig. 4c). The NOE observed between OMe1 and C20H [Fig. 4b, distance observed in the crystal structure d(OMe1–C20H) = 2.8 Å)] further supports the S(6)-type H-bonding since such an arrangement will provide space for the OMe1 to have a NOE with C20H due to their proximity.

Thus, it can be concluded from the 2D NOESY studies on the dimer **3a** that the molecule retains the non-planar structural architecture caused by steric hindrance and shows additionally the S(6)-type hydrogen bonding, which was not visible in the solid-state structure, presumably due to solid-state packing effects (Fig. 2a).

In the higher order analog **4**, the same sterically driven conformational organization can be observed in solution, according to the NOE patterns (Fig. 5). As already found for **3a**, NH1 shows a stronger NOE with OMe1 than with OMe2, and NH3 shows a stronger dipolar coupling with OMe3 than with OMe2 (Fig. 5a). In addition, the NHs show strong coupling with the aromatic protons (NH1 *vs* C20H, NH2 *vs* C32H, and NH3 *vs* C44H, Fig. 5b) suggesting close proximity. Similarly, the inter-residue interactions of OMe with aromatic protons (OMe1 *vs* C20H, OMe2 *vs* C32H, and OMe3 *vs* C44H, Fig. 5c) provide further support for the existence of a non-planar arrangement of the naphthyl rings in the higher oligomer **4**.

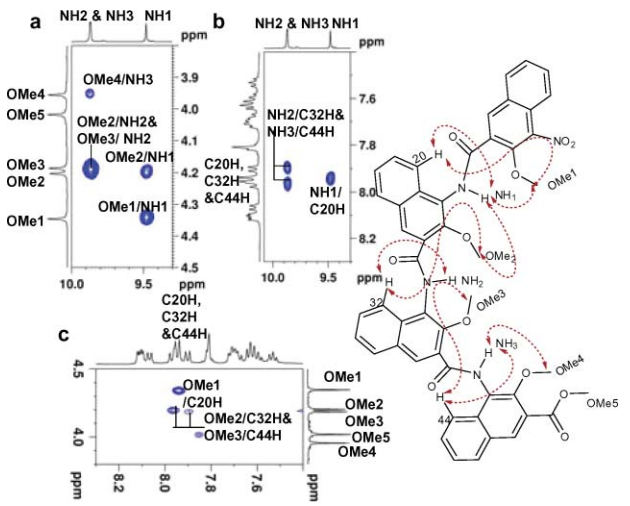


Fig. 5 2D extracts of oligomer **4** (500 MHz, $CDCl_3$). (a) NH *vs* OMe; (b) NH *vs* ArH; (c) OMe *vs* ArH.

In the 2D NOESY studies of the dimer **7a**, a strong dipolar coupling between the amide NH and OMe1 indicates their close proximity, facilitating the formation of the expected S(6)-type intramolecular hydrogen bonding (Fig. 6a). The results obtained in the dilution as well as the titration experiments support this intramolecular hydrogen bonding (Fig. S3–S4†). Furthermore, the NOE between OMe1 *vs* C21H, NH and C21H, and NH *vs* C14H suggest an anti-periplanar arrangement of the naphthyl rings with S(6)-type hydrogen bonding, as supposed.

The NOE patterns (Fig. 7) for the larger oligomer **8** are completely in line with the conformational features of the shorter oligomer **7a**. In **8**, all the amide NHs show strong inter-residue

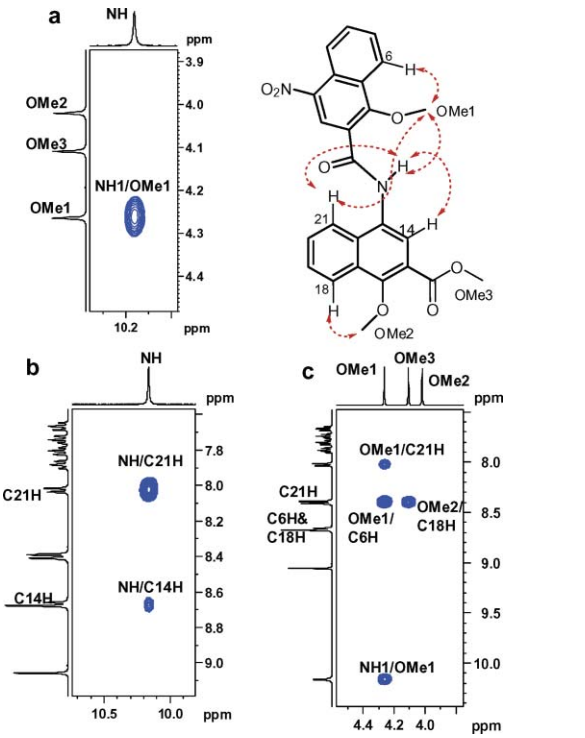


Fig. 6 2D NOESY extracts of **7a** (500 MHz, $CDCl_3$). (a) NH *vs* OMe; (b) NH *vs* ArH; (c) OMe *vs* ArH.

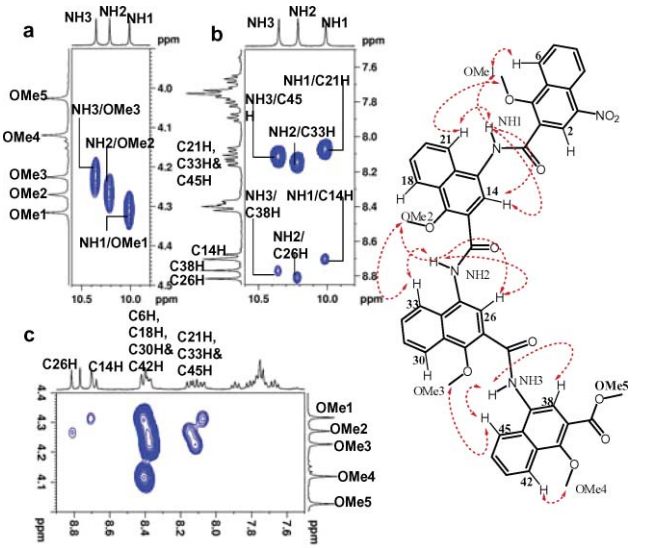


Fig. 7 2D NOESY extracts of **8** (400 MHz, $CDCl_3$). (a) NH *vs* OMe; (b) NH *vs* ArH; (c) OMe *vs* ArH.

NOEs to the methoxy groups (NH1 *vs* OMe1, NH2 *vs* OMe2, NH3 *vs* OMe3, Fig. 7a) suggesting their close proximity as presupposition for the formation of S(6)-type hydrogen bonding. The dipolar interactions of the NHs with both *peri* protons of the naphthyl ring and with the *ortho* protons (NH1 *vs* C21H, NH1 *vs* C14H, NH2 *vs* C33H, NH2 *vs* C26H, NH3 *vs* C45H, NH3 *vs* C38H, Fig. 8b) strongly indicate the anti-periplanar arrangement of the adjacent naphthyl rings,[18] as already seen in **7a**.

The anti-periplanar arrangement of the naphthyl rings paves the way for the closer positioning of the alkoxy methyls to the *peri*

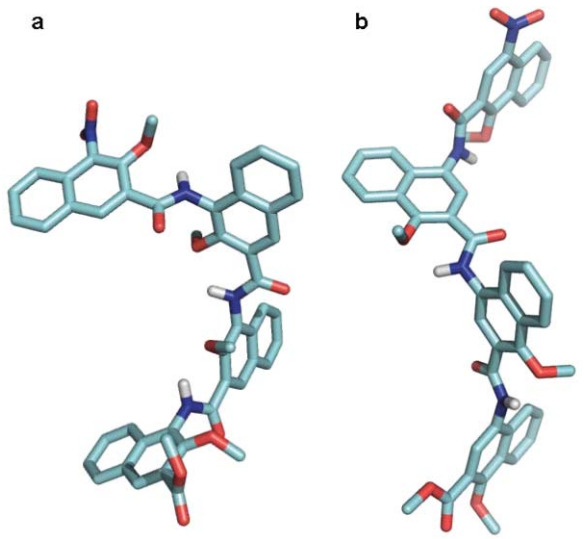


Fig. 8 Structural architecture of oligomers **4** (a) and **8** (b) at the HF/6-31G* level of *ab initio* MO theory, displaying the nonplanar arrangement of the naphthyl rings.

protons of the naphthyl ring nearby, resulting in NOEs (OMe1 *vs* C21H, OMe2 *vs* C33H, and OMe3 *vs* C45H, Fig. 7c). This is also responsible for the inter-residual NOEs between alkoxy methyls and *ortho* protons of the adjacent naphthyl rings (OMe1 *vs* C14H, OMe2 *vs* 26H, Fig. 7c). Summarizing the solution-state NMR data, it can be concluded that all oligomers exist in a sterically driven non-planar well defined conformation stabilized by S(6)-type hydrogen bonding.

Quantum chemical studies

The difficulties in crystallizing the higher order oligomers **4** and **8** prompted us to investigate their structural architecture by *ab initio* MO theory at the HF/6-31G* level (for details of the calculations, see ESI†). *Ab initio* MO theory at this level has considerably contributed to the understanding of the structure of peptidic and aromatic foldamers and has been able to predict numerous structures which were experimentally found afterwards.[19] Due to the steric and hydrogen bonding effects in our oligomers, the conformational space is very restricted and predetermined.

The sterically enforced non-planarity of the adjacent naphthyl rings (anti-periplanar arrangement), as observed in the crystal structure of the shorter analogs **3a** and **7a**, is reflected in the higher-order oligomers **4** and **8**, respectively (Fig. 8a,b). The *ab initio* structures are consistent with the S(6)-type intramolecular hydrogen bonding in the higher order oligomers **4** and **8**, indicated in the solution-state NMR studies. Both oligomers form helical structures, which differ significantly due to the different positioning of the hydrogen bond-directing alkoxy oxygens appended on the naphthyl rings.

Conclusions

In summary, we have reported the synthesis of novel naphthalene homo-oligoamides that display an anti-periplanar arrangement of the naphthyl rings primarily induced by steric interactions between adjacent groups and functionalities. The structural investigations of these homo-oligoamides, both in the solid and solution state, support the selected design strategy. In all cases, the oligomer backbone adopts a non-planar conformation with an anti-periplanar arrangement of the adjacent rings as confirmed by single-crystal X-ray diffraction studies, solution-state NMR studies, and theoretical calculations. Steric interactions and hydrogen bonding play the determining role in modulating the conformation of these synthetic oligomers. The results of this study suggest that steric interactions can be used for the rational design of novel synthetic oligomers displaying structural architectures different from those classically observed.

Experimental procedures

Methyl-3-methoxy-4-nitro-2-naphthoate 2a

Methyl-3-hydroxy-4-nitro-2-naphthoate (5 g, 20 mmol, 1 equiv.) in acetone (100 mL) was subjected to *O*-methylation using dimethylsulfate (3.9 mL, 40 mmol, 2 equiv.) and K_2CO_3 (5.6 g, 40 mmol, 2 equiv.). After stirring at room temperature for 12 h, the reaction mixture was filtered. The filtrate was evaporated under reduced pressure. The residue obtained was taken up in dichloromethane (150 mL), and washed with dilute HCl. Drying and purification by column chromatography (eluent: 15% AcOEt/pet. ether, R_f: 0.4) furnished **2a** as a yellow solid (5.12 g, 97%). mp: 72–73 °C; (Found: C, 59.88; H, 4.32, N, 5.28. Calc. for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36%.); ν_{max} ($CHCl_3$)/(cm^{-1}): 3024, 2951, 1732, 1636, 1537, 1499, 1450, 1356, 1340, 1290, 1242, 1215, 1161, 1148, 1088; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.60 (s, 1H, ArH), 7.99–7.94 (m, 1H, ArH), 7.72–7.60 (m, 3H, ArH), 4.03 (s, 3H, OMe), 4.02 (s, 3H, OMe); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 164.6, 148.1, 142.7, 135.5, 130.9, 129.1, 129.0, 127.1, 126.8, 123.5, 120.8, 64.4, 52.7; ESI MS: 284.02 $(M + Na)^+$.

3-Methoxy-4-nitro-2-naphthoic acid 2b

The ester **2a** (2 g, 7.7 mmol) in methanol (10 mL) was subjected to ester hydrolysis using 2 N LiOH solution. After completion of the reaction (12 h), the pale yellow precipitate obtained on acidification of the reaction mixture was filtered, washed with water till the pH was neutral. The residue obtained was dried in P_2O_5 desiccator yielding the free acid **2b** quantitatively. This was used for further reaction without purification.

Methyl-4-amino-3-methoxy-2-naphthoate 2c

The amine **2c** was obtained by reduction of the nitro group in **2a** (2 g, 7.7 mmol) using H_2 (60 psi), Pd/C (90 mg) in AcOEt. After the complete consumption of starting material (6 h), the reaction mixture was filtered through a pad of Celite. The filtrate was evaporated and dried to give the amine **2c** which was used for the next reaction without further purification.

Methyl-3-methoxy-4-(3-methoxy-4-nitro-2-naphthamido)-2-naphthoate 3a

To a solution containing acid **2b** (2 g, 8 mmol, 1 equiv.) and amine **2c** (1.87 mg, 8 mmol, 1 equiv.) in dichloromethane (20 mL), DCC (2.0 g, 9.6 mmol, 1.2 equiv.) and HOBt (cat. amount) were added.

The reaction mixture was allowed to stir at 0 °C for 10 min and for 12 h at room temperature. The DCU was filtered off and the filtrate was washed sequentially with sat. solution of sodium bicarbonate, potassium hydrogen sulfate solution, and water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to give the crude product which on purification by column chromatography (eluent: AcOEt/pet. ether 20 : 80, R_f: 0.3) afforded **3a** as a yellow solid (2 g, 55%), which could be crystallized from a solution of ethyl acetate and pet. ether; mp: 177–178 °C; Found: C, 65.28; H, 4.46; N, 6.02. Calc. for $C_{25}H_{20}N_2O_7$: C, 65.21; H, 4.38; N, 6.08%.); ν_{max} ($CHCl_3$)/(cm^{-1}): 3365, 3018, 1728, 1674, 1628, 1537, 1506, 1358, 1298, 1213, 1045, 1001; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.34 (s, 1H, NH), 8.94 (s, 1H, ArH), 8.46 (s, 1H, ArH), 8.05-8.03 (d, J = 8.03 Hz, 1H, ArH), 7.93-7.91 (d, J = 8.03 Hz, 1H, ArH), 7.84-7.82 (d, J = 8.28 Hz, 1H, ArH), 7.76 (m, 2H, ArH), 7.67-7.51 (m, 3H, ArH), 4.28 (s, 3H, OCH_3), 4.01 (s, 3H, $COOCH_3$), 3.94 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.9, 163.3, 151.9, 146.8, 142.1, 135.8, 133.1, 132.6, 130.9, 129.9, 129.8, 129.5, 129.4, 129.0, 127.6,126.9, 126.1, 125.7, 125.2, 123.6, 123.3, 121.0, 65.1, 62.6, 52.5; ESI MS: 461.29 $(M + H)^+$, 483.30 $(M + Na)^+$, 499.28 $(M + K)^+$;

3-Methoxy-4-(3-methoxy-4-nitro-2-naphthamido)-2-naphthoic acid 3b

The compound **3a** (0.9 g, 1.9 mmol) in dioxane (10 mL) was subjected to ester hydrolysis using 2 N LiOH solution. After completion of the reaction, the pale yellow precipitate obtained on acidification of the reaction mixture was filtered, washed with water till the pH was neutral, and the residue obtained was dried over P_2O_5 in a desiccator to yield the acid **3b** quantitatively. This was used for further reaction without purification.

Methyl 4-(4-amino-3-methoxy-2-naphthamido)-3-methoxy-2-naphthoate 3c

The dimer **3a** (0.95 g, 2 mmol) was subjected to the reduction of its nitro group using H_2 (60 psi) and Pd/C (90 mg) in AcOEt. After the complete consumption of starting material (6 h), the reaction mixture was filtered through a pad of Celite. The filtrate was evaporated and dried to give the amine **3c**, which was used for the next reaction without further purification.

Methyl 3-methoxy-4-(3-methoxy-4-(3-methoxy-4-(3-methoxy-4-nitro-2-naphthamido)-2-naphthamido)-2-naphthamido)-2-naphthoate 4

The acid **3b** (0.3 g, 0.7 mmol, 1 equiv.) was converted to the corresponding acid chloride **3d** using oxalyl chloride (0.1 mL, 2.1 mmol, 3 equiv.) and DMF (cat. amount) in dichloromethane. After 3 h, the solvent and excess oxalyl chloride were evaporated under reduced pressure. The residue obtained was taken up in dichloromethane (10 mL) and was added to a solution containing amine **3c** (0.29 g, 0.7 mmol, 1 equiv.) and triethylamine (0.28 mL, 2.1 mmol, 3 equiv.) in dichloromethane (5 mL) and the reaction mixture was allowed to stir for 12 h at room temperature. The solvent was removed under reduced pressure. The crude product obtained was purified by column chromatography (chloroform/AcOEt 90:10 R_f: 0.5) yielding **4** (0.23, 40%); mp: 228–230 °C; Found: C, 68.62; H, 4.58; N, 6.46. Calc. for $C_{49}H_{38}N_4O_{11}$: C, 68.52; H, 4.46; N, 6.52%.); ν_{max} ($CHCl_3$)/(cm^{-1}): 3238, 3020, 1724, 1651, 1632, 1599, 1502, 1460, 1416, 1217, 1153, 1038, 1003; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.84 (s, 2H, NH), 9.45 (s, 1H, NH), 9.03 (s, 1H, ArH), 8.98 (s, 1H, ArH), 8.92 (s, 1H, ArH), 8.46 (s, 1H, ArH), 8.11-8.04 (m, 3H, ArH), 7.96-7.87 (m, 4H, ArH), 7.79 (m, 2H, ArH), 7.71-7.49 (m, 7H, ArH), 4.33 (s, 3H, OCH_3), 4.18 (s, 3H, OCH_3), 4.17 (s, 3H, OCH_3), 4.00 (s, 3H, $COOCH_3$), 3.93 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.0, 164.5, 164.4, 163.3, 151.8, 151.2, 146.8, 142.2, 136.2, 133.9, 133.4, 132.9, 132.85, 132.8, 132.7, 131.2, 130.7, 130.6, 130.1, 129.9, 129.7, 129.3, 129.0, 128.9, 127.8, 127.1, 126.7, 126.5, 126.4, 126.1, 125.8, 125.3, 124.7, 124.6, 124.5, 124.7, 124.6, 124.5, 123.7, 123.3, 122.9, 121.1, 64.9, 63.1, 62.6, 52.5; ESI MS: 859.86 $(M + H)^+$; 881.89 $(M + Na)^+$; 897.76 $(M + K)^+$.

Methyl-1-methoxy-4-nitro-2-naphthoate 6a

1-Hydroxy-2-naphthoic acid **5** (6 g, 31.5 mmol, 1 equiv.) in acetone (200 mL) was subjected to simultaneous esterification and *O*-methylation using dimethyl sulfate (9.7 mL, 95.7 mmol, 3 equiv.) and K_2CO_3 (13.2 g, 95.7 mmol, 3 equiv.). After refluxing for 8 h, the solid was removed by filtration and the residue obtained on evaporation of the filtrate was taken up in dichloromethane. The organic layer was washed sequentially with sat. sodium bicarbonate, dilute HCl, and water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and the filtrate was subjected to careful nitration using conc. HNO_3 and conc. H_2SO_4 (cat. amount.), at 0 °C. The progress of the reaction was monitored by TLC, and after the completion of the reaction the organic layer was washed with sat. sodium bicarbonate and then with water. The crude product obtained after the removal of solvent was purified by column chromatography (eluent: 15% AcOEt/pet. ether, R_f: 0.4) affording **6a** as a yellow solid (7.3 g, 88%). mp: 106 °C; (Found: C, 59.72; H, 4.28; N, 5.48. Calc. for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36.%); ν_{max} ($CHCl_3$)/(cm^{-1}): 3020, 2955, 1728, 1626, 1564, 1524, 1506, 1445, 135, 1323, 1279, 1234, 1215, 1157, 1090; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.77 (s, 1H, ArH), 8.70-8.65 (m, 1H, ArH), 8.46-8.41 (m, 1H, ArH), 7.89-7.69 (m, 2H, ArH), 4.16 (s, 3H, OCH_3), 4.03 (s, 3H, $COOCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 164.5, 162.8, 141.5, 131.6, 129.5, 128.1, 127.8, 126.5, 124.3, 123.5, 116.9, 64.0, 52.7; ESI-MS 261.07 $(M + H)^+$, 284.04 $(M + Na)^+$.

1-Methoxy-4-nitro-2-naphthoic acid 6b

The ester **6a** (2 g, 7.7 mmol) in methanol (15 mL) was subjected to ester hydrolysis using 2 N LiOH solution. After completion of the reaction, the pale yellow precipitate obtained on acidification of the reaction mixture was filtered, washed with water till the pH was neutral, and the residue obtained was dried in P_2O_5 desiccator to yield the acid **6b** quantitatively. This was used for further reaction without purification.

Methyl-4-amino-1-methoxy-2-naphthoate 6c

The compound **6a** (2 g, 7.7 mmol) was subjected to reduction of its nitro group using H_2 (60 psi), Pd/C (90 mg) in AcOEt. After the complete consumption of starting material (6 h), the reaction mixture was filtered through a pad of Celite. The filtrate

was evaporated and dried to give the amine **6c** which was used for the next reaction without further purification.

Methyl-1-methoxy-4-(1-methoxy-4-nitro-2-naphthamido)-2-naphthoate 7a

To a solution containing the acid **6b** (2 g, 8 mmol, 1 equiv.) and amine **6c** (1.88 g, 8 mmol, 1 equiv.) in acetonitrile (15 mL), HBTU (2.96 g, 9.2 mmol, 1.2 equiv.) was added followed by DIEA (1.6 mL, 9.2 mmol, 1.2 equiv.). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure, diluted with dichloromethane (50 mL), and the organic layer was washed with sat. sodium bicarbonate. The crude product obtained after removal of the solvent was purified by column chromatography (eluent: 20% AcOEt/pet. ether, R_f: 0.3) affording **7a** as a yellow solid (3 g, 85%); mp: 205–206 °C; (Found: C, 65.18; H, 4.44; N, 6.18. Calc. for $C_{25}H_{20}N_2O_7$: C, 65.21; H, 4.38; N, 6.08%.); ν_{max}(nujol)/(cm^{-1}): 3274, 3018, 1716, 1643, 1550, 1516, 1458, 1377, 1229, 1155, 1085, 1003; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.14 (s, 1H, NH), 9.02 (s, 1H, ArH), 8.65-8.63 (m, 2H, ArH), 8.38-8.36 (d, J = 8.28 Hz, 2H, ArH), 8.02-8.00 (d, J = 8.53 Hz, 1H, ArH), 7.87-7.62 (m, 4H, ArH), 4.24 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 4.00 (s, 3H, $COOCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.9, 161.9, 159.1, 156.0, 143.4, 131.4, 130.1, 129.2, 129.0, 128.5, 128.34, 128.3, 128.2, 126.8, 126,.0, 124.6, 124.0, 123.6, 121.4, 120.9, 120.6, 119.1, 64.6, 63.5, 52.3; ESI MS: 461.03 $(M + H)^+$, 483.07 $(M + Na)^+$, 499.04 $(M + K)^+$.

1-Methoxy-4-(1-methoxy-4-nitro-2-naphthamido)-2-naphthoic acid 7b

To a solution containing **7a** (1 g, 2.2 mmol, 1 equiv.) in dioxane (10 mL) $LiOH{\cdot}H_2O$ (0.19 g, 4.4 mmol, 2 equiv.) in water (5 mL) was added. After completion of the reaction, the yellow precipitate obtained on acidification of the reaction mixture was filtered, washed with water till the pH was neutral, and the residue obtained was dried in P_2O_5 desiccator to yield the acid **7b** quantitatively. This was used for the next reaction without further purification.

Methyl 4-(4-amino-1-methoxy-2-naphthamido)-1-methoxy-2-naphthoate 7c

The compound **7a** (1 g, 2.2 mmol, 1 equiv.) was subjected to reduction of its nitro group using H_2 (60 psi), Pd/C (100 mg) in AcOEt. After the complete consumption of starting material, the reaction mixture was filtered through a pad of Celite. The filtrate was evaporated and dried to give the amine **7c** which was used for the next reaction without further purification.

Methyl 1-methoxy-4-(1-methoxy-4-(1-methoxy-4-(1-methoxy-4-nitro-2-naphthamido)-2-naphthamido)-2-naphthamido)-2-naphthoate 8

The acid **7b** (0.5 g, 1.1 mmol, 1 equiv.) and the amine **7c** (0.48 g, 1.1 mmol, 1 equiv.) were taken up in acetonitrile (15 mL). HBTU (0.5 g, 1.3 mmol, 1.2 equiv.) and DIEA (0.23 mL, 1.3 mmol, 1.2 equiv.) were added and the reaction mixture was stirred at 60 °C for 12 h at room temperature. The crude product obtained after work-up was purified by column chromatography (chloroform/AcOEt: 90:10 R_f: 0.5) yielding **8** as a yellow solid (43%). mp: 235–237 °C; (Found: C, 68.72, H, 4.60, N, 6.30. Calc. for $C_{49}H_{38}N_4O_{11}$: C, 68.52; H, 4.46; N, 6.52.); ν_{max} (nujol)/(cm^{-1}): 3234, 2922, 2852, 1722, 1639, 1462, 1377, 1312, 1227, 1151, 1086; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.34 (s, 1H, NH), 10.20 (s, 1H, NH), 10.00 (s, 1H, NH), 9.05 (s, 1H, ArH), 8.79 (s, 1H, ArH), 8.75 (s, 1H, ArH), 8.68-8.65 (m, 2H, ArH), 8.40-8.35 (m, 4H, ArH), 8.14-8.05 (m, 3H, ArH), 7.89-7.85 (t, J = 7.35 Hz, 1H, ArH), 7.80-7.70 (m, 6H, ArH), 7.67-7.63 (t, J = 7.61 Hz, 1H, ArH), 4.29 (s, 3H, OCH_3), 4.25 (s, 3H, OCH_3), 4.20 (s, 3H, OCH_3), 4.10 (s, 3H, OCH_3), 4.0 (s, 3H, $COOCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1, 163.8, 163.6, 162.4, 159.3, 155.6, 153.9, 153.2, 143.7, 139.3, 131.6, 130.5, 13.2, 129.9, 129.2, 129.1, 128.9, 128.8, 128.7, 128.4, 128.3, 127.3, 127.2, 126.7, 126.1, 124.6, 124.1, 123.8, 123.7, 122.4, 122.2, 122.1, 121.3, 121, 120.5, 119.3, 114.1, 64.6, 64.1, 64.0, 60.4, 52.3; MALDI-TOF: 859.35 $(M + H)^+$.

Acknowledgements

PP is thankful to CSIR, New Delhi, for a research fellowship. GJS thanks the International Foundation for Science (IFS, Sweden), Grant No. F/4193-1 for financial support. HJH thanks Deutsche Forschungsgemeinschaft (HO2346/1–3 and SFB 610) for continuous financial support.

References

1 (*a*) *Foldamers: Structure, Properties and Applications*, ed. S. Hecht and I. Huc, Wiley-VCH, Weinheim, Germany, 2007; (*b*) S. H. Gellman, *Acc. Chem. Res.*, 1998, **31**, 173; (*c*) K. D. Stigers, M. J. Soth and J. S. Nowick, *Curr. Opin. Chem. Biol.*, 1999, **3**, 714; (*d*) M. D. Smith and G. W. J. Fleet, *J. Peptide Sci.*, 1999, **5**, 425; (*e*) K. Kirshenbaum, R. N. Zuckermann and K. A. Dill, *Curr. Opin. Struct. Biol.*, 1999, **9**, 530; (*f*) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes and J. S. Moore, *Chem. Rev.*, 2001, **101**, 3893; (*g*) R. P. Cheng, S. H. Gellman and W. F. DeGrado, *Chem. Rev.*, 2001, **101**, 3219; (*h*) M. S. Cubberley and B. L. Iverson, *Curr. Opin. Chem. Biol.*, 2001, **5**, 650; (*i*) D. Seebach, A. K. Beck and D. J. Bierbaum, *Chem. Biodiversity*, 2004, **1**, 1111; (*j*) R. S. Roy and P. Balaram, *J. Peptide Res.*, 2004, **63**, 279; (*k*) A. R. Sanford, K. Yamato, X. Yang, L. Yuan, Y. Han and B. Gong, *Eur. J. Biochem.*, 2004, **271**, 1416; (*l*) G. Licini, L. J. Prins and P. Scrimin, *Eur. J. Org. Chem.*, 2005, 969; (*m*) Z.-T. Li, J.-Li. Hou, C. Li and H.-P. Yi, *Chem. Asian. J.*, 2006, **1**, 766; (*n*) A. D. Bautista, C. J. Craig, E. A. Harker and A. Schepartz, *Curr. Opin. Chem. Biol.*, 2007, **11**, 685; (*o*) C. M. Goodmaan, S. Choi, S. Shandler and W. F. DeGrado, *Nature Chemical Biology*, 2007, **3**, 252; (*p*) W. S. Horne and S. H. Gellman, *Acc. Chem. Res.*, 2008, **41**, 1399; (*q*) C. E. Schafmeister, Z. Z. Brown and S. Gupta, *Acc. Chem. Res.*, 2008, **41**, 1387.

2 For recent articles, see: (*a*) K. Gademann, M. Ernst, D. Hoyer and D. Seebach, *Angew Chem. Int. Ed. Engl.*, 1999, **38**, 1223; (*b*) D. Liu and W. F. DeGrado, *J. Am. Chem. Soc.*, 2001, **123**, 7553; (*c*) A. Tanatani, M. J. Mio and J. S. Moore, *J. Am. Chem. Soc.*, 2001, **123**, 1792; (*d*) G. N. Tew, D. Liu, B. Chen, R. J. Doerksen, J. Kaplan, P. J. Carroll, M. L. Klein and W. F. DeGrado, *PNAS.*, 2002, **99**, 5110; (*e*) J. T. Ernst, J. Becerril, H. S. Park, H. Yin and A. D. Hamilton, *Angew. Chem. Int. Ed.*, 2003, **42**, 535; (*f*) C. G. Levins and C. E. Schafmeister, *J. Am. Chem. Soc.*, 2003, **125**, 4703; (*g*) R. F. Epand, T. L. Raguse, S. H. Gellman and R. M. Epand, *Biochemistry*, 2004, **43**, 9527; (*h*) M. Inouye, M. Waki and H. Abe, *J. Am. Chem. Soc.*, 2004, **126**, 2022; (*i*) J. M. Heemstra and J. S. Moore, *J. Am. Chem. Soc.*, 2004, **126**, 1648; (*j*) S. Choi, D. J. Clements, V. Pophristic, I. Ivanov, S. Vemparala, J. S. Bennett, M. L. Klein, J. D. Winkler and W. F. DeGrado, *Angew. Chem. Int. Ed.*, 2005, **44**, 6685; (*k*) Y. A. Fillon, J. P. Anderson and J. Chmielewski, *J. Am. Chem. Soc.*, 2005, **127**, 11798; (*l*) C. Dolain, C. Zhan, J.-M. Léger, L. Daniels and I. Huc, *J. Am. Chem. Soc.*, 2005, **127**, 2400; (*m*) N. G. Angelo and P. S. Arora, *J. Am. Chem. Soc.*, 2005, **127**, 17134; (*n*) F. Zhang, S. Bai, G. P. A. Yap, V. Tarwade and J. M. Fox, *J. Am. Chem. Soc.*, 2005, **127**, 10590; (*o*) A. Khan, C. Kaiser and S. Hecht, *Angew. Chem. Int. Ed.*, 2006, **45**, 1878; (*p*) A. J. Nicoll, D. J. Miller, K. Futterer,

R. Ravelli and R. K. Allemannn, *J. Am. Chem. Soc.*, 2006, **128**, 9187; (*q*) H. P. Yi, J. Wu, K.-L. Diang, X.-K. Jiang and Z.-T. Li, *J. Org. Chem.*, 2007, **72**, 870.

3 For recent articles on biotic oligomers, see: (*a*) D. Seebach, M. Overhand, F. N. M. Kuehnle, B. Martinoni, L. Oberer, U. Hommel and H. Widmer, *Helv. Chim. Acta*, 1996, **79**, 913; (*b*) D. H. Appella, L. A. Christianson, D. A. Klein, M. A. Richards, D. R. Powell and S. H. Gellman, *J. Am. Chem. Soc.*, 1999, **121**, 7574; (*c*) D. Yang, B. Li, F.-F. Ng, Y.-L. Yan, J. Qu and Y.-D. Wu, *J. Org. Chem.*, 2001, **66**, 7303; (*d*) T. D. W. Claridge, D. D. Long, C. M. Baker, B. Odell, G. H. Grant, A. A. Edwards, G. E. Tranter, G. W. J. Fleet and M. D. Smith, *J. Org. Chem.*, 2005, **70**, 2082; (*e*) A. Violette, M. C. Averlant-Petit, V. Semetey, C. Hemmerlin, R. Casimir, R. Graff, M. Marruad, J.-P. Briand, D. Rognan and G. Guichard, *J. Am. Chem. Soc.*, 2005, **127**, 2156; (*f*) G. Srinivasulu, S. Kiran, Kumar, G. V. M. Sharma and A. C. Kunwar, *J. Org. Chem.*, 2006, **71**, 8395; (*g*) M. A. Schmitt, S. H. Choi, I. A. Guzei and S. H. Gellman, *J. Am. Chem. Soc.*, 2006, **128**, 4538; (*h*) G. V. M. Sharma, V. B. Jadhav, K. V. S. Ramakrishna, P. Jayaprakash, K. Narsimulu, V. Subash and A. C. Kunwar, *J. Am. Chem. Soc.*, 2006, **128**, 14657.

4 For recent articles on abiotic oligomers, see: (*a*) J. C. Nelson, J. G. Saven, J. S. Moore and P. G. Wolynes, *Science*, 1997, **277**, 1793; (*b*) H. Jiang, J.-M. Léger and I. Huc, *J. Am. Chem. Soc.*, 2003, **125**, 3448; (*c*) J. J. van Gorp, J. A. J. M. Vekemans and E. W. Meijer, *Chem. Comm.*, 2004, 60; (*d*) X. Yang, L. Yuan, K. Yamato, A. L. Brown, W. Feng, M. Furukawa, X. C. Zeng and B. Gong, *J. Am. Chem. Soc.*, 2004, **126**, 3148; (*e*) E. R. Gillies, C. Dolain, J.-M. Léger and I. Huc, *J. Org. Chem.*, 2006, **71**, 7931.

5 (*a*) J. Zhu, R. D. Parra, H. Zeng, E. Skrzypczak-Jankun, X. C. Zeng and B. Gong, *J. Am. Chem. Soc.*, 2000, **122**, 4219; (*b*) L. Yuan, H. Zeng, K. Yamato, A. R. Sanford, W. Feng, H. S. Atreya, D. K. Sukumaran, T. Szyperski and B. Gong, *J. Am. Chem. Soc.*, 2004, **126**, 16528; (*c*) I. Huc, *Eur. J. Org. Chem.*, 2004, 17; (*d*) B. Gong, *Acc. Chem. Res.*, 2008, 2008, **41**, 1376.

6 (*a*) C. Li, S.-F. Ren, J.-L. Hou, H.-P. Yi, S.-Z. Zhu, X.-K. Jiang and Z.-T. Li, *Angew. Chem. Int. Ed.*, 2005, **44**, 5725; (*b*) Z.-T. Li, J.-H. Hou and C. Li, *Acc. Chem. Res.*, 2008, **41**, 1343.

7 (*a*) Y. Hamuro, S. J. Geib and A. D. Hamilton, *J. Am. Chem. Soc.*, 1996, **118**, 7529; (*b*) H. Jiang, J.-M. Léger and I. Huc, *J. Am. Chem. Soc.*, 2003, **125**, 3448.

8 Owing to its directionality and specificity, hydrogen bonds play an important role in stabilizing the secondary structures. See: (*a*) A. Tanatani, H. Kagechika, I. Azumaya, R. Fukutomi, Y. Ito, K. Yamaguchi and K. Shudo, *Tetrahedron Lett.*, 1997, **38**, 4425; (*b*) V. Berl, I. Huc, R. Khoury, M. J. Krische and J.-M. Lehn, *Nature*, 2000, **407**, 720; (*c*) X. Yang, S. Martinovic, R. D. Smith and B. Gong, *J. Am. Chem. Soc.*, 2003, **125**, 9932; (*d*) S. D. Pol, C. Zorn, C. D. Klein, O. Zerbe and O. Reiser, *Angew. Chem. Int. Ed.*, 2004, **43**, 511; (*e*) C. A. Hunter, A. Spitaleri and S. Tomas, *Chem. Comm.*, 2005, 3691.

9 J.-M. Lehn, A. Rigault, J. Siegel, J. Harrowfield, B. Chevrier and D. Moras, *PNAS.*, 1987, **84**, 2565.

10 (*a*) K. Tanaka, T. Furuta, K. Fuji, Y. Miwa and N. Taga, *Tetrahedron: Asymmetry*, 1996, **7**, 2199; (*b*) K. Tsubaki, M. Miura, H. Morikawa, H. Tanaka, T. Kawabata, T. Furuta, K. Tanaka and K. Fuji, *J. Am. Chem. Soc.*, 2003, **125**, 16200; (*c*) P. K. Baruah, R. Gonnade, P. R. Rajamohanan, H.-J. Hofmann and G. J. Sanjayan, *J. Org. Chem.*, 2007, **72**, 5077.

11 H.-P. Yi, C. Li, J.-Li. Hou, X.-K. Jiang and Z.-T. Li, *Tetrahedron*, 2005, **61**, 7974.

12 Naphthalene- and anthracene-based oligomers with iminodicarbonyl linkers have been reported. See: H. Masu, I. Mizutani, T. Kato, I. Azumaya, K. Yamaguchi, K. Kishikawa and S. Kohmoto, *J. Org. Chem.*, 2006, **71**, 8037.

13 P. A. Wender, T. C. Jessop, K. Pattabiraman, E. T. Pelkey and C. L. VanDeusen, *Org. Lett.*, 2001, **3**, 3229.

14 The crystal structure was solved by direct methods and refined by full-matrix least-squares on F^2 for all data using SHELXTL software. The hydrogen atom of hydroxy group was located on the difference map and refined isotropically. Other hydrogen atoms were refined in the riding mode†.

15 (*a*) S. Grimme, *Angew. Chem. Int. Ed.*, 2008, **47**, 3430; (*b*) E. C. Lee, D. Kim, P. Jurečka, P. Tarakeshwar, P. Hobza and K. S. Kim, *J. Phys. Chem. A*, 2007, **111**, 3446.

16 (*a*) H. Tang, R. J. Doerksen, T. V. Jones, M. L. Klein and G. N. Tew, *Chemistry & Biology*, 2006, **13**, 427; (*b*) P. Prabhakaran, V. G. Puranik and G. J. Sanjayan, *J. Org. Chem.*, 2005, **70**, 10067.

17 For recent references, see: (*a*) D. Yang, D.-D. Zhang, Y. Hao, Y.-D. Wu, S.-W. Luo and N.-Y. Zhu, *Angew. Chem. Int. Ed.*, 2004, **116**, 6887; (*b*) F. Chen, N.-Y. Zhu and D. Yang, *J. Am. Chem. Soc.*, 2004, **126**, 15980; (*c*) P. K. Baruah, N. K. Sreedevi, B. Majumdar, R. Pasricha, P. Poddar, R. Gonnade, S. Ravindranathan and G. J. Sanjayan, *Chem. Comm.*, 2008, 712.

18 For a general review on the peri-effect in naphthalenes, see: V. Balasubramaniayan, *Chem. Rev.*, 1966, **66**, 567.

19 (*a*) Y.-D. Wu and D.-P. Wang, *J. Am. Chem. Soc.*, 1998, **120**, 13485; (*b*) D. Zanuy, C. Alemán and S. Muñoz-Guerra, *Int. J. Biol. Macromolecules*, 1998, **23**, 175; (*c*) K. Möhle and H.-J. Hofmann, *J. Pept. Res.*, 1998, **51**, 19; (*d*) K. Möhle, R. Günther, M. Thormann, N. Sewald and H.-J. Hofmann, *Biopolymers*, 1999, **50**, 167; (*e*) Y.-D. Wu and D.-P. Wang, *J. Am. Chem. Soc.*, 1999, **121**, 9352; (*f*) R. Günther and H.-J. Hofmann, *J. Am. Chem. Soc.*, 2001, **123**, 247; (*g*) R. Günther and H.-J. Hofmann, *Helv. Chim. Acta*, 2002, **85**, 2149; (*h*) X. Yang, A. L. Brown, M. Furukawa, S. Li, W. E. Gardinier, E. J. Bukowski, F. V. Bright, C. Zheng, X. C. Zeng and B. Gong, *Chem. Comm.*, 2003, 56; (*i*) C. Baldauf, R. Günther and H.-J. Hofmann, *Helv. Chim. Acta*, 2003, **86**, 2573; (*j*) T. Beke, I. G. Csizmadia and A. Perczel, *J. Comput. Chem.*, 2004, **25**, 285; (*k*) C. Baldauf, R. Günther and H.-J. Hofmann, *Angew. Chem. Int. Ed.*, 2004, **43**, 1594; (*l*) C. Baldauf, R. Günther and H.-J. Hofmann, *J. Org. Chem.*, 2004, **69**, 6214; (*m*) C. Baldauf, R. Günther and H.-J. Hofmann, *Biopolymers*, 2005, **80**, 675; (*n*) A. S. Norgren and P. I. Arvidsson, *Org. Biomol. Chem.*, 2005, **3**, 1359; (*o*) C. Baldauf, R. Günther and H.-J. Hofmann, *J. Org. Chem.*, 2005, **70**, 5351; (*p*) C. Baldauf, R. Günther and H.-J. Hofmann, *Phys. Biol.*, 2006, **3**, S1–S9; (*q*) C. Baldauf, R. Günther and H.-J. Hofmann, *J. Org. Chem.*, 2006, **71**, 1200; (*r*) T. Buffeteau, L. Ducasse, L. Poniman, N. Delsuc and I. Huc, *Chem. Comm.*, 2006, 2714; (*s*) A. M. Kendhale, R. Gonnade, P. R. Rajamohanan, H.-J. Hofmann and G. J. Sanjayan, *Chem. Comm.*, 2008, 2541.

20 Crystallographic data of **3a** and **7c** have been deposited with the CCDC with numbers 691283 and 691284, respectively. Data were collected at $T = 293$ K on SMART APEX CCD. **3a**: A colorless needle, approximate size $0.19 \times 0.05 \times 0.01$ mm, was used for data collection. $C_{25}H_{20}N_2O_7$, $M = 460.43$, orthorhombic, $Pna2_1$, $a = 27.786(2)$, $b = 4.5194(8)$, $c = 17.0553(4)$ Å, $V = 2141.7(4)$ Å^3, $Z = 4$, $D_c = 1.428$ g/cm^3, $\mu(\mathrm{MoK}\alpha) = 0.106$ mm^{-1}, 16929 reflections measured, 3772 unique [$I > 2\sigma(I)$], R value 0.0350, $wR2 = 0.0751$. **7c**: A colourless needle, of approximate size $0.11 \times 0.08 \times 0.03$ mm, was used for data collection. $C_{25}H_{22}N_2O_5{\cdot}CHCl_3$, $M = 549.81$, triclinic, $P\bar{1}$, $a = 10.1275(13)$, $b = 10.7976(14)$, $c = 11.7307(14)$ Å, $\alpha = 96.883(3)$, $\beta = 94.267(3)$, $\gamma = 90.920(3)°$, $V = 1269.6(3)$ Å^3, $Z = 2$, $D_c = 1.438$ g/cm^3, $\mu(\mathrm{MoK}\alpha) = 0.402$ mm^{-1}, 8097 reflections measured, 2861 unique [$I > 2\sigma(I)$], R value 0.0607, $wR2 = 0.1060$.