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Synthetic duplex oligomers: optimizing interstrand affinity through the use of a noncovalent constraint

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Abstract—The covalent casting of a one-dimensional hydrogen-bonding motif permits the design of oligomers possessing a predetermined duplex mode of aggregation. In this account, studies on the hydrogen bond mediated self-assembly of dimeric duplex oligomers **2** in solution are described. Two-fold self-association in solution is established by ^{1}H NMR, and the intended mode of assembly is further corroborated via X-ray crystallographic analysis. An increase in interstrand affinity of over three orders of magnitude is observed upon substitution of nitrogen for oxygen in the oligomer backbone, owing to preorganization of the molecular strand in the binding effective conformation as directed by the formation of an internal hydrogen bond. These data provide insight into the structural and interactional features of the oligomers required for high affinity/specificity binding in organic media.

1. Introduction

In nature, functional nanostructures are assembled from biomacromolecular precursors such as proteins and DNA. Such biomacromolecules possess exceptional mechanical properties (e.g. arachnid silk fibers),[1] remarkable catalytic functions (e.g. cytochrome-p450),[2] and high-density information storage capabilities (e.g. CD-ROM technology $\sim 10^8$ bits/cm^2 versus DNA $\sim 10^{21}$ bits/cm^3).[3] With such inspiration from nature, it is not surprising that a broad goal of modern research relates to understanding the key factors that govern self-assembly events. Such studies have primarily focused on the assembly of small molecular precursors.[4] In contrast, few rational approaches to the directed organization of oligomeric precursors have been forthcoming.[5,6,7] As part of a general investigation into the assembly of molecular strands, we have introduced the 'covalent casting' of one-dimensional hydrogen-bonded superstructures as a general strategy toward oligomers of *predetermined* topography, specifically a duplex mode of aggregation.[6,8] By developing technologies for the induction of predefined higher order structural motifs via self-assembly of oligomeric and polymeric precursors, steps are taken toward the definition of a platform for the de novo design of abiotic polymer-based devices of nanometric dimensions, which, upon sufficient development, may embody capabilities beyond those displayed by their natural counterparts.

Here, we explore the structural and interactional features of synthetic duplex oligomers required for high affinity/specificity binding. We begin by optimizing the self-association of the simplest oligomer, duplex dimer **2**, in solution. These studies reveal that an ostensibly modest structural modification of the oligomer backbone, the substitution of oxygen for nitrogen, produces an increase in interstrand affinity of greater than *three orders of magnitude*. This effect owes to preorganization of the oligo-aminotriazine in the form of an internal hydrogen bond.

2. Results and discussion

In order to selectively direct the aggregation of polyvalent oligomers, subtle manipulation of the myriad weak forces contributing to the overall binding event is required. For the design of topographically defined molecular strands, we make use of the noncovalent connectivities defined by known one-dimensional hydrogen bonding motifs as 'blueprints' for the introduction of commensurate covalent scaffolding.[6] For example, in the solid state, 2-amino-4,6-dichlorotriazine yields a ribbon **I** comprised of hydrogen-bonded dimers. An inter-chlorine distance of ca 3.3 Å between alternate triazines of ribbon **I** was obtained from X-ray crystallographic data.[8] The supramolecular framework may be 'covalently cast' by connecting alternate aminotriazines with 1,3-diol or 1,3-aminoalcohol linkages. In this way, covalent strands **III** are devised, which are structurally encoded with a highly selective interactional algorithm, i.e. the expression of the duplex superstructure **II** (Scheme 1).

Optimum interstrand affinity requires engineering structural

Keywords: hydrogen bonding; self-assembly; foldamer; polymer structure; duplex oligomer.

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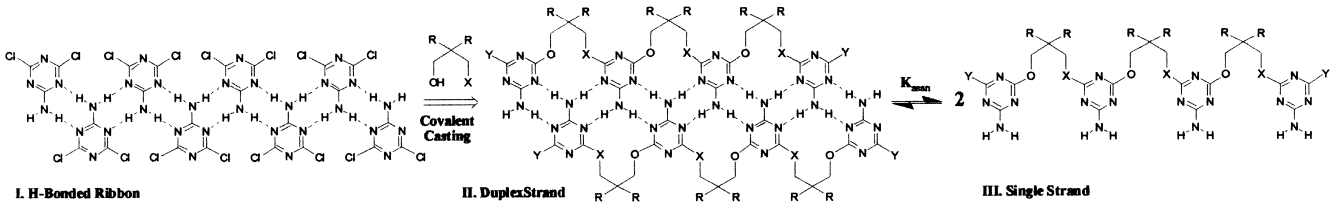


Scheme 1. Covalent casting of the one-dimensional H-bonding motif **I** obtained upon self-assembly of 2-amino-4,6-dichlorotriazine through the introduction of linking groups. The resulting duplex strand **II** exists in equilibrium with the single-stranded oligomer **III**.

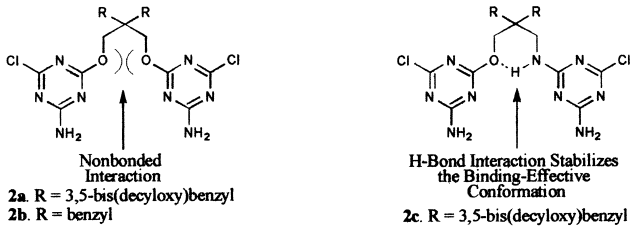
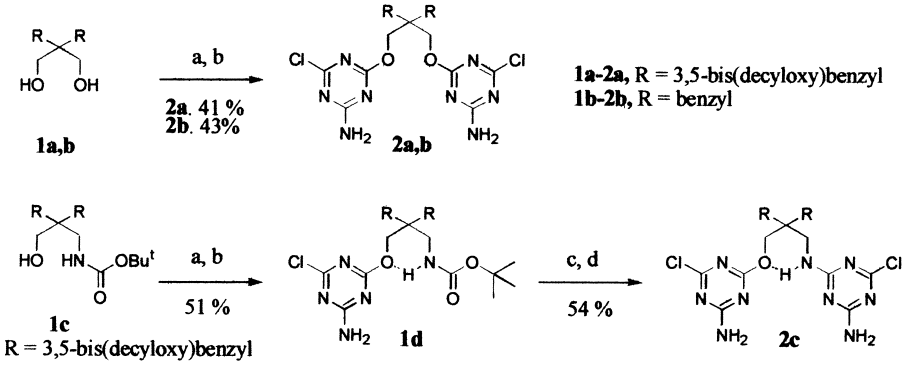


Figure 1. An internal NH···OH-bond preorganizes aminoalcohol-linked oligotriazines.

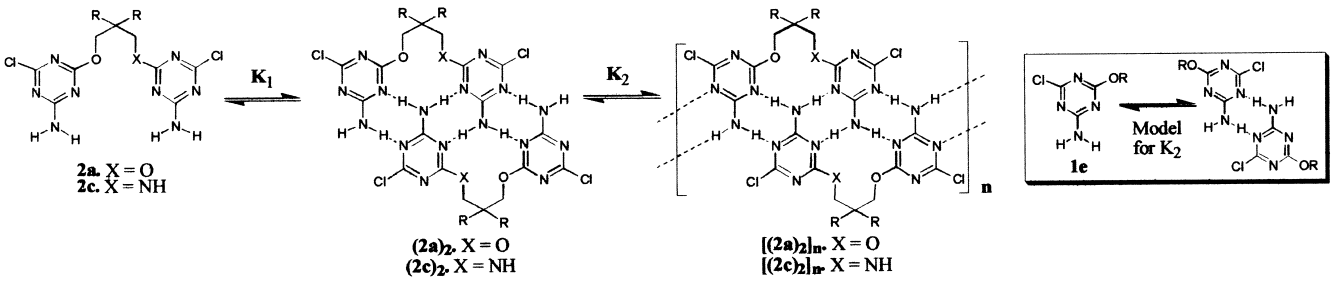
features of the oligomer backbone to enhance the population of binding-effective conformers. Geminal substitution of the inter-triazine linking group should promote adoption of the requisite *syn*-periplanar geometry via Thorpe–Ingold effect.[9] However, in the case of 1,3-diol linking groups, a *syn*-periplanar arrangement elicits unfavorable steric and electrostatic interactions due to eclipsed C–O bonds. The *nonbonded* interactions evident in the diol-linked dimers **2a** and **2b** may be transformed into *bonded* interactions through the utilization of an aminoalcohol linking group as in **2c**, which embodies an intramolecular NH···O hydrogen bond (Fig. 1).

For the synthesis of the dimeric duplex oligomers **2a**–**2c**, it was desirable to develop a convergent, modular sequence that would allow access to a series of analogues in preparative quantities. The diol-linked bis-aminotriazines **2a** and **2b** were prepared using our previously described synthetic protocol.[8] Thus, 1,3-diols **1a** and **1b**, obtained via alkylation of diethyl malonate followed by $LiAlH_4$ reduction, were exposed to cyanuric chloride. Aminolysis of the resulting triazinylated diols provides **2a** and **2b**. The preparation of the aminoalcohol-linked bis-aminotriazine **2c** requires sequential triazinylation of the BOC-protected amino-alcohol **1c**, which is prepared via alkylation of ethyl cyano-acetate followed by $LiAlH_4$ reduction and, finally, N-protection. Treatment of **1c** with cyanuric chloride followed by exposure to ammonia gives the mono-amino-triazine **1d**. Removal of the BOC-group unmasks the latent amine nucleophile, which upon exposure to 2-amino-4,6-dichlorotriazine yields **2c** (Scheme 2).

The interstrand affinity of aminotriazine oligomers may be estimated by the determination of association constants via ^1H NMR dilution studies (see Fig. 3 for a representative ^1H NMR dilution plot).[10,11] For the diol-linked bis-amino-triazine **2a**, self-association occurs through the action of



Scheme 2. Synthesis of diol-and aminoalcohol-linked aminotriazine dimers **2a**–**2c**. *Reagents*: (a) cyanuric chloride, 2,6-lutidine, DCM, reflux (b) anhydrous NH_3, 25°C (c) HCl, 1,4-dioxane, CH_2Cl_2, 25°C (d) 2-amino-4,6-dichloro-[1,3,5]triazine, $i Pr_2NEt$, $CHCl_3$, reflux.



Scheme 3. Self-assembly of monomer **1e** and dimers **2a** and **2c**.

Table 1. Association constants (M^{-1}) determined by ^1H NMR

Compound	Percent d^6-DMSO in $CDCl_3$ (v:v)		
	0%	5%	10%
1e	2.9	–	–
2a	100	9.2	2.0
2c	ND[a]	28,000	1100

[a] Dissociation was not observed within the detection limits of ^1H NMR.

six hydrogen bonds (Scheme 3). Dilution studies performed at room temperature fit a two-fold self-association model with low error, yielding the following dimerization constant in neat $CDCl_3$: $\log(K_1)=2.0\pm0.10$ ($K_1=100\ M^{-1}$) (Table 1). The intended duplex mode of assembly was corroborated via X-ray crystallographic analysis of the structurally related 2,2-dibenzyl-1,3-diol-linked species **2b** (Fig. 2). This association constant is relatively low for a complex bound by six hydrogen bonds. To confirm that **2a** was not aggregating through the formation of only two hydrogen bonds, dilution studies were performed on mono-triazine **1e**. An association constant of $\log(K_1)=0.46\pm0.026$ ($K_1=2.9\ M^{-1}$) was obtained in the same medium (Table 1). The disparity between association constants obtained for **1c** and **2a**, in addition to the crystal structure of **2a**, support the proposed mode of assembly. While an association constant corresponding to the oligomerization of $(\mathbf{2a})_2$ to yield $[(\mathbf{2a})_2]_n$ (i.e. K_2) could not be extracted from the dilution data, compound **1c** may also serve as a model for the estimation of K_2.

In principle, the low binding constant observed for **2a** might stem from unfavorable secondary electrostatic interactions between adjacent hydrogen bond donor–acceptor pairs[12] and sub-optimal pK_a matching.[13] However, as previously outlined, diminished interstrand affinity was anticipated for **2a** on the basis of steric and electrostatic repulsion between oxygen atoms incurred upon adoption of the binding-effective conformation. For aminoalcohol-linked dimer **2c**, nonbonded interactions evident in **2a** are exchanged for bonded interactions. Consequently, higher binding affinities should result. Upon dilution in neat $CDCl_3$, negligible changes in chemical shift for all signals of **2c** were observed, suggesting the persistence of the duplex $(\mathbf{2c})_2$ at the detection limits of the ^1H NMR experiment. In order to witness dissociation of the duplex in a concentration range suitable for NMR studies, a more competitive medium was required. Therefore, dilution studies were performed in d^6-DMSO/$CDCl_3$.[14] For the aminoalcohol-linked dimer **2c**, dilution in 5% d^6-DMSO/$CDCl_3$ (v:v) yielded an association constant of $\log(K_1)=4.45\pm0.56$ ($K_1=28{,}000\ M^{-1}$). This value is more than three orders of magnitude greater than that observed for the analogous diol-linked dimer **2a** in the same medium, $\log(K_1)=0.96\pm0.06$ ($K_1=9.2\ M^{-1}$). Dilution studies performed on **2c** in 10% d^6-DMSO/$CDCl_3$ (v:v) yielded an association constant of $\log(K_1)=3.1\pm0.20$ ($K_1=1100\ M^{-1}$), whereas the diol-linked species **2a** yielded an association constant of $\log(K_1)=0.32\pm0.02$ ($K_1=2.0\ M^{-1}$). In this case, aminoalcohol-linked bis-aminotriazine **2c** exhibits an association constant more than two orders of magnitude greater than the diol-linked species **2a** (Fig. 3).

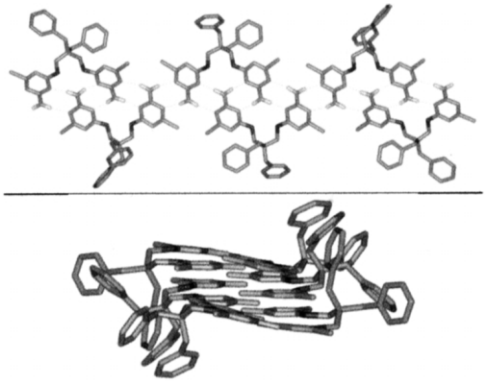


Figure 2. X-Ray crystal structure of **2b** revealing the encoded duplex mode of association. Top: view orthogonal to the plane of the H-bonded tape. Bottom: view along the plane defined by the H-bonded tape revealing the eclipsed C–O bonds of the diol linkage.

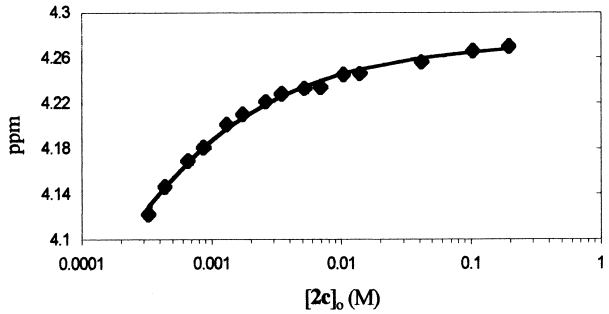


Figure 3. A representative ^1H NMR dilution plot. Chemical shift values of the methylene protons adjacent to the oxygen atom in the linker or aminoalcohol-linked dimer **2c** were monitored as a function of [**2c**] in 5% d^6-DMSO/$CDCl_3$ (v:v). The curved line represents the calculated fit of the experimental data points.

The profound increase in interstrand affinity observed for aminoalcohol-linked bis-aminotriazine **2c** deserves some comment. For **2c**, preorganization of the binding residues is induced through the action of a noncovalent constraint. For covalently constrained systems, the reduction of entropic terms is offset by an enthalpic penalty if the binding sites are restricted to a sub-optimal geometry.[15] Noncovalent interactions are weak and, hence, are amenable to considerable distortion accompanied by minimal loss in energy.[16] As such, noncovalent constraints should allow for an 'induced fit' between binding residues. While we have yet to compare **2c** to a covalently constrained analogue, an induced fit between strands may account for the dramatic increase in interstrand affinity.

3. Conclusion and outlook

The covalent casting of one-dimensional hydrogen bonding motifs represents an effective and rational strategy toward molecular strands that embody predefined modes of assembly. Here, we establish duplex formation in solution and demonstrate that fine-tuning of the structural and interactional features of the oligomer backbone can produce profound increases in complex stability. Through the covalent casting of alternative one-dimensional hydrogen bonding motifs, it should be possible to design a diverse set of duplex oligomers that assemble via mutually orthogonal

modes of recognition. Ultimately, conjugation of 'orthogonal' strand segments will enable the creation of information-rich oligomers capable of sequence specific hybridization.

4. Experimental

4.1. General

Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl prior to use. Dichloromethane was distilled from P_2O_5 prior to use as a reaction medium. Deuterated solvents were used as received from Cambridge Isotope Laboratories.

Analytical TLC was performed on EM Reagents 0.25 mm silica gel 60-F plates, and visualized under UV light. Flash chromatography was performed on silica gel 60 (200–400 mesh). NMR spectra were recorded on a Varian UNITY+ 300 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained at 300 and 75 MHz, respectively. FT-IR spectra were taken on a Nicolet Impact 410 spectrometer. Melting points were obtained on a Thomas–Hoover Unimelt apparatus and are uncorrected.

4.1.1. 4-(3,5-Bis-decyloxy-benzyloxy)-6-chloro-[1,3,5]triazin-2-ylamine (1e). (3,5-Bis-decyloxy-phenyl)-methanol[17] (3.57 g, 8.49 mmol, 100 mol%), cyanuric chloride (1.96 g, 10.6 mmol, 125 mol%), and *i*Pr$_2$NEt (2.19 g, 16.9 mmol, 200 mol%) were dissolved in CH_2Cl_2 (80 mL, 0.11 M), and the mixture was stirred at ambient temperature for 6 h. The reaction mixture was then washed with brine, dried over Na_2SO_4, evaporated onto silica gel, and purified chromatographically (SiO_2: 5% ethyl acetate in hexanes) to provide 2-(3,5-bis-decyloxy-benzyloxy)-4,6-dichloro-[1,3,5]-triazine (2.50 g, 52%). ^{1}H NMR: (δ, ppm, $CDCl_3$) 0.86 (t, J=6.6 Hz, 6H), 1.21–1.43 (m, 30H), 1.74 (quintet, J=6.6 Hz, 4H), 3.90 (t, J=6.7 Hz, 4H), 5.41 (s, 2H), 6.41 (m, 1H), 6.53 (m, 2H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 14.4, 20.3, 22.9, 26.3, 29.4, 29.6, 29.7, 29.8, 29.9, 32.1, 68.4, 71.9, 102.0, 106.9, 135.9, 160.8, 171.1, 172.8; HRMS: calcd for $C_{30}H_{47}N_3O_3Cl_2$: 567.2994, found 567.2988. To a solution of 2-(3,5-bis-decyloxy-benzyloxy)-4,6-dichloro-[1,3,5]triazine (1.00 g, 1.76 mmol, 100 mol%) in Et_2O (20 mL, 0.088 M) was added a solution of NH_3 (2 M in *i*PrOH, 2.00 mL, 4.00 mmol, 220 mol%), and the mixture stirred at ambient temperature for 30 min. The reaction mixture was washed with H_2O and brine, dried over Na_2SO_4, filtered, and evaporated to dryness, to afford **1e** as a white solid (0.869 g, 90%). ^{1}H NMR: (δ, ppm, $CDCl_3$) 0.86 (t, J=6.6 Hz, 6H), 1.25–1.45 (m, 28H), 1.73 (quintet, J=6.6 Hz, 4H), 3.90 (t, J=6.6 Hz, 4H), 5.29 (s, 2H), 5.95 (br s, 1H), 6.38 (m, 1H), 6.51 (m, 2H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 14.1, 22.6, 25.9, 29.1, 29.2, 29.3, 29.5, 29.6, 31.8, 68.0, 69.7, 101.2, 106.2, 137.1, 160.4, 168.2, 170.7, 171.2; FT-IR (neat, cm^{-1}): 3506, 3324, 3188, 2922, 2844, 1662, 1604, 1565, 1533, 1468, 1422, 1344, 1305, 1247, 1156, 1059, 1000, 935, 812, 728, 676; mp 71–74°C.

4.1.2. [3-(4-Amino-6-chloro-[1,3,5]triazin-2-yloxy)-2,2-bis-(3,5-bis-decyloxy-benzyl)-propyl]-carbamic acid *tert*-butyl ester (1d). To a solution of [2-(3,5-bis-decyloxy-benzyl)-3-(3,5-bis-decyloxy-phenyl)-2-hydroxymethyl-propyl]-carbamic acid *tert*-butyl ester **1c**[18] (4.00 g, 4.08 mmol, 100 mol%) in toluene (100 mL, 0.04 M) was added 2,6-lutidine (0.83 mL, 7.12 mmol, 175 mol%) followed by cyanuric chloride (1.20 g, 6.51 mmol, 160 mol%). The resulting orange mixture was stirred and heated to 80°C under N_2 for 18 h. The mixture was then diluted with toluene and washed with citric acid (15% aqueous solution) and brine. The organic layer was treated with activated charcoal, dried over Na_2SO_4 and was filtered through celite and concentrated in vacuo, yielding an amber oil (5.90 g). The oily residue was dissolved in CH_2Cl_2 (50 mL) and treated with NH_3 (2.0 M solution in *i*PrOH, 8 mL, 16.0 mmol, 400 mol%). After 3 h stirring at ambient temperature, the mixture was diluted with dichloromethane and washed with H_2O and brine, then dried with Na_2SO_4, filtered, and concentrated in vacuo. The resulting amber oil was purified by column chromatography (SiO_2: 10% ethyl acetate in hexanes). Evaporation of the pure fractions yielded **1d** as a waxy solid (2.29 g, 51%). R_f=0.65 (25% ethyl acetate in hexanes). ^{1}H NMR: (δ, ppm, $CDCl_3$) 0.85 (t, J=6.6 Hz, 12H), 1.24–1.4 (m, 66H), 1.40 (s), 1.70 (quintet, J=6.4 Hz, 8H), 2.67 (A part of AB system, J=13.8 Hz, 2H), 2.74 (B part of AB system, J=13.8 Hz, 2H), 3.17 (d, J=4.9 Hz, 2H), 3.82 (t, J=6.7 Hz, 8H), 4.05 (s, 2H), 4.65 (br s, 1H), 6.25 (s, 4H), 6.29 (s, 2H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 14.1, 22.7, 26.0, 28.3, 29.2, 29.3, 29.4, 29.5, 29.6, 31.9, 40.8, 42.3, 43.0, 68.0, 79.4, 99.7, 108.9, 115.9, 138.7, 156.0, 160.1, 168.1, 170.8; HRMS: calcd for $C_{65}H_{111}N_5O_7Cl$: 1108.8172, found: 1108.8165; FT-IR: (neat, cm^{-1}) 3327, 3210, 2920, 2846, 1704, 1649, 1600, 1563, 1532, 1464, 1415, 1371, 1297, 1248, 1155, 1063, 1014, 939, 902, 835, 804, 717 cm^{-1}; mp 46–50°C.

4.1.3. 1,3-Bis-(4-amino-6-chloro-[1,3,5]triazin-2-yloxy)-2,2-bis-(3,5-bis-decyloxy-benzyl)-propane (2a). Prepared in 41% overall yield from 2,2-bis-(3,5-bis-decyloxy-benzyl)-propane-1,3-diol **1a**[19] as described for **2b**. The title compound was obtained as an oil. R_f=0.2 (20% ethyl acetate in hexanes); ^{1}H NMR: (δ, ppm, $CDCl_3$) 0.85 (t, J=6.6 Hz, 12H), 1.23–1.40 (m, 60H), 1.70 (quintet, J=6.6 Hz, 8H), 2.79 (s, 4H), 3.81 (t, J=6.4 Hz, 8H), 4.31 (s, 4H), 6.24 (m, 4H), 6.30 (m, 2H), 7.22 (br s, 2H), 8.12 (br s, 2H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 14.1, 22.7, 26.0, 29.2, 29.3, 29.4, 29.6, 31.9, 41.6, 68.0, 108.9, 137.9, 160.1, 167.9, 170.5, 171.1; HRMS: calcd for $C_{63}H_{103}N_8O_6Cl_2$: 1137.7378, found: 1137.7373; FT-IR: (neat, cm^{-1}) 3582, 3222, 2920, 2836, 1679, 1596, 1512, 1467, 1416, 1358, 1313, 1249, 1152, 1062, 998, 934, 812 cm^{-1}.

4.1.4. 1,3-Bis-(4-amino-6-chloro-[1,3,5]triazin-2-yloxy)-2,2-dibenzyl-propane (2b). Cyanuric chloride (14.4 g, 77.9 mmol, 400 mol%) was added to a solution of 2,2-dibenzyl-propane-1,3-diol **1b**[19] (5.00 g, 19.5 mmol, 100 mol%) and 2,6-lutidine (8.36 g, 78.0 mmol, 400 mol%) in CH_2Cl_2 (100 mL, 0.2 M). The red–orange mixture was stirred at reflux under N_2 for 15 h, then washed with brine, dried over $MgSO_4$, filtered and concentrated to dryness in vacuo. The residue was purified by column chromatography (SiO_2: 25% hexanes in CH_2Cl_2) to afford 1,3-bis-(4,6-dichloro-[1,3,5]triazin-2-yloxy)-2,2-dibenzyl-propane as a yellow solid (9.40 g, 87%). R_f=0.6 (25% ethyl

acetate in hexanes); ^{1}H NMR: (δ, ppm, $CDCl_3$) 3.04 (s, 4H), 4.28 (s, 4H), 7.15 (m, 4H), 7.28 (m, 6H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 38.3, 42.3, 70.2, 127.0, 128.6, 130.4, 135.5, 170.6, 172.7; HRMS: calcd for $C_{23}H_{19}N_6O_2Cl_4$: 551.0323, found: 551.0320; FT-IR: (neat, cm^{-1}) 3125, 3055, 2913, 2836, 2354, 1711, 1544, 1506, 1441, 1384, 1313, 1261, 1178, 1062, 857, 812, 741, 696 cm^{-1}; mp 148–157°C. Ammonia (0.5 M in 1,4-dioxane, 130 mL, 65 mmol, 400 mol%) was added to a solution of 1,3-bis-(4,6-dichloro-[1,3,5]triazin-2-yloxy)-2,2-dibenzyl-propane (8.9 g, 16.1 mmol, 100 mol%) in Et_2O (50 mL, 0.32 M). The mixture was stirred for 45 min at which point the reaction was washed with water and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated in vacuo to ca. 20 mL. The gradual addition of hexanes produced a white precipitate, which was collected by suction filtration to yield pure **2b** (4.08 g, 49%). ^{1}H NMR: (δ, ppm, DMSO-d_6) 2.85 (s, 4H), 3.92 (s, 4H), 7.07–7.28 (m, 10H), 8.00 (s, 2H), 8.05 (s, 2H); ^{13}C NMR: (δ, ppm, DMSO-d_6) 38.4, 41.8, 66.4, 67.6, 126.6, 128.4, 130.3, 136.2, 168.0, 169.9, 170.1; HRMS: calcd for $C_{23}H_{23}N_8O_2Cl_2$: 513.1231, found: 513.1317; FT-IR: (neat, cm^{-1}) 3350, 3286, 3183, 3132, 2367, 2328, 1750, 1679, 1634, 1512, 1403, 1294, 1242, 1139, 1069, 979, 921, 754, 702, 664, 587 cm^{-1}; mp 210–214°C.

4.1.5. 1-(4-Amino-6-chloro-[1,3,5]triazin-2-yloxy)-2,2-bis(3,5-bis-decyloxy-benzyl)-3-(4-amino-6-chloro-[1,3,5]-triazin-2-ylamino)-propane (2c). A solution of hydrogen chloride (4.0 M in 1,4-dioxane, 1.35 mL, 5.40 mmol, 400 mol%) was added under N_2 to a solution of **1d** (1.50 g, 1.35 mmol, 100 mol%) in CH_2Cl_2 (50 mL, 0.027 M). After 6 h, the volatiles were removed under reduced pressure and the residue was maintained on a vacuum line for 30 min. The white solid residue was dissolved in DMF (20 mL) and 2-amino-4,6-dichloro-[1,3,5]triazine (0.445 g, 2.70 mmol, 200 mol%) was added, followed by *i*Pr_2NEt (1.17 mL, 6.75 mmol, 500 mol%). After heating to 60°C under N_2 for 1 h, the mixture was allowed to cool spontaneously to ambient temperature and stirred for an additional 15 h. The reaction mixture was poured into H_2O to give a precipitate that was extracted into Et_2O. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated to dryness in vacuo to yield a waxy solid (1.46 g). Chromatographic purification (SiO_2: 10% *i*PrOH in hexanes) yielded **2c** (0.82 g, 54%) along with several mixed fractions. R_f=0.4 (10% *i*PrOH in hexanes). ^{1}H NMR: (δ, ppm, 7.9 mM in $CDCl_3$) 0.85 (t, J=6.9 Hz, 12H), 1.23–1.39 (m, 57H), 1.72 (m, 8H), 2.60 (A part of AB system, J=13.5 Hz, 2H), 2.72 (B part of AB system, J=13.5 Hz, 2H), 3.52 (br s, 0.5H), 3.62 (br s, 1.4H), 3.84 (br s, 8H), 4.12 (br s, 0.3H), 4.38 (br s, 1.4H), 5.82 (br s, 1H), 6.19 (s, 4H), 6.32 (s, 2.5H); ^{13}C NMR: (δ, ppm, $CDCl_3$) 14.1, 22.7, 26.0, 29.3, 29.5, 29.6, 31.9, 40.4, 68.0, 99.7, 109.1, 137.9, 160.1; HRMS: calcd for $C_{63}H_{104}N_9O_5Cl_2$: 1136.7537, found: 1136.7565; FT-IR: (neat, cm^{-1}) 3444, 3302, 3136, 2926, 2846, 2636, 2365, 2136, 1890, 1692, 1643, 1587, 1464, 1415, 1353, 1303, 1155, 1063, 939, 841, 798 cm^{-1}; mp 140–145°C.

References

1. (a) Qu, Y.; Payne, S. C.; Apkarian, R. P.; Conticello, V. P. *J. Am. Chem. Soc.* **2000**, *122*, 5014. For a review, see: (b) Deming, T. *J. Adv. Mater.* **1997**, *9*, 299.
2. For a review, see: Loew, G. H.; Harris, D. L. *Chem. Rev.* **2000**, *100*, 407.
3. Martin, P. J. Photochromism. In *Introduction to Molecular Electronics*, Petty, M. C., Bryce, M. R., Bloor, D., Eds.; Oxford University: New York, 1995; pp. 114–117.
4. For selected reviews, see: (a) Philp, D.; Stoddart, J. F. *Angew. Chem. Int. Ed.* **1996**, *35*, 1155. (b) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229. (c) Langford, S. J.; Stoddart, J. F. *Pure Appl. Chem.* **1996**, *68*, 1255. (d) Fuhrhop, J.-H.; Rosengarten, B. *Synlett* **1997**, 1015. (e) Krische, M. J.; Lehn, J.-M. *Struct. Bonding* **2000**, *94*, 3. (f) Zimmerman, S. C.; Corbin, P. S. *Struct. Bonding* **2000**, *94*, 63.
5. For reviews, see: (a) Gellman, S. H. *Acc. Chem. Res.* **1998**, *31*, 173. (b) Moore, J. *Acc. Chem. Res.* **1997**, *30*, 402. (c) Archer, E. A.; Gong, H.; Krische, M. J. *Tetrahedron* **2000**, *57*, 1139.
6. Archer, E. A.; Sochia, A. E. Krische. *Chem. Eur. J.* **2001**, *10*, 2059.
7. For duplex oligomers reported from other labs, see: (a) Bisson, A. P.; Carver, F. J.; Eggleston, D. S.; Haltiwanger, R. C.; Hunter, C. A.; Livingstone, D. L.; McCabe, J. F.; Rotger, C.; Rowan, A. E. *J. Am. Chem. Soc.* **2000**, *122*, 8856. (b) Corbin, P. S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **2000**, *122*, 3779. (c) Zeng, H.; Miller, R. S.; Flowers, R. A.; Gong, B. *J. Am. Chem. Soc.* **2000**, *122*, 2635.
8. Archer, E. A.; Goldberg, N. T.; Lynch, V.; Krische, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 5006.
9. (a) Schleyer, P. V. R. *J. Am. Chem. Soc.* **1961**, *83*, 1368. (b) Jung, M. E. *Synlett* **1999**, 843.
10. (a) Chen, J.-S.; Shirts, R. B. *J. Phys. Chem.* **1985**, *89*, 1643. (b) Chen, J.-S.; Rosenberger, F. *Tetrahedron Lett.* **1990**, *31*, 3975.
11. Dimerization constants were obtained from ^{1}H NMR dilution data using the computer program CHEMEQUI developed by Dr Vitaly Solov'ev. For a detailed description, see: Solov'ev, V. P.; Baulin, V. E.; Strakhova, N. N.; Kazachenko, V. P.; Belsky, V. K.; Varnek, A. A.; Volkova, T. A.; Wipff, G. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1489.
12. (a) Pranata, J.; Wierschke, S. G.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1991**, *113*, 2810. (b) Jorgensen, W. L.; Pranata, J. *J. Am. Chem. Soc.* **1990**, *112*, 2008.
13. (a) Garcia-Viloca, M.; Gonzalez-Lafont, A.; Lluch, J. M. *J. Phys. Chem. A* **1997**, *101*, 3880. (b) Chen, J.; McAllister, M. A.; Lee, J. K.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 4611.
14. Mammen, M.; Simanek, E. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1996**, *118*, 12614.
15. Sharp, K. *Prot. Sci.* **2001**, *10*, 661 and references therein.
16. (a) Taylor, R.; Kennard, O. *Acc. Chem. Res.* **1984**, *17*, 320. (b) Scheiner, S. *Acc. Chem. Res.* **1994**, *27*, 402.
17. Prepared in analogy to a published procedure: Johansson, G.; Percec, V.; Ungar, G.; Abramic, D. *J. Chem. Soc. Perkin Trans. 1* **1994**, 447.
18. Prepared in analogy to a published procedure: Varie, D. L.; Shih, C.; Hay, D. A.; Andis, S. L.; Corbett, T. H.; Gossett, L. S.; Janisse, S. K.; Martinelli, M. J.; Moher, E. D.; Schultz, R. M.; Toth, J. E. *Bioorg. Med. Chem. Lett.* **1999**, *9* (3), 369.
19. Prepared in analogy to a published procedure: Czech, B. P.; Zazulak, W.; Kumar, A.; Dalley, N. K.; Weiming, J.; Bartsch, R. A. *J. Heterocycl. Chem.* **1991**, *28*, 1387.