Oligoanthranilamides. Non-Peptide Subunits That Show Formation of Specific Secondary Structure

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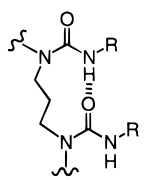
Abstract: A family of novel oligomers based on the anthranilamide nucleus has been prepared and shown to form well-defined secondary structural features. ^{1}H NMR and X-ray crystallographic techniques have demonstrated that intramolecular hydrogen bonds play a key role in stabilizing both linear sheet and helical conformational forms.

Introduction

The modular construction and structural diversity of proteins provides a paradigm for the design of new molecules with controlled conformations and defined functions. Repeating α-amino acids subunits form regions of ordered secondary structure such as α-helices and β-sheets which in turn provide the scaffolding onto which binding or catalytic groups are linked.[1] Intramolecular hydrogen bonds between amide groups in the peptide backbone play a critical role in stabilizing secondary structural regions. A key feature of α-amino acids as building blocks is that small modifications in form and sequence can lead to shifts in the intramolecular hydrogen bonding pattern and so generate a wide range of protein tertiary structures.

In the past few years there has considerable interest in the preparation of new materials based on modular designs and constructed from families of variable monomers. In some cases structural integrity of the materials has been maintained by using rigid components such as the [1,1,1]bicyclopentanes of Michl[2] or the [2,2,2]bicyclooctanes of Zimmerman.[3] In others interlocking rings, as in Stoddart's catenanes,[4] rigidify the superstructure. A particularly attractive approach for the construction of molecular scaffolding is to emulate the biological strategy of using intramolecular hydrogen bonding to control conformation.[5] This has the advantage of allowing a modular approach with high yielding amide or ester bond forming steps but with rigidity imposed by directed hydrogen bonds in place of polycyclic structures.[6] Nowick has recently shown that intramolecular hydrogen bonds can be used to control the structure of oligourea scaffolds,[7] as in **1**, and Schreiber has demonstrated the formation of both helical and sheet structures using vinylogous amino acids,[8] **2**. A series of peptide-derived oligocarbamates[9] reported by Schultz, and vinylogous sulfonamides[10] recently reported by Gennari, may also exploit intramolecular hydrogen bonds in the formation of folded conformations.



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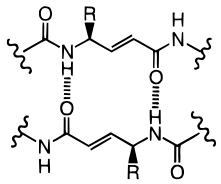

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Our interest lay in developing a simple family of molecular components that could be connected in different ways to give a range of compact and well-defined secondary structures. Several factors can be employed to contribute to the relative stability of these folded conformations including: (a) intramolecular hydrogen bonding between adjacent or distant subunits, (b) π-stacking between subunits, (c) rigidification, where possible, of the subunits to minimize conformational freedom and torsional strain in the folded state, and (d) destabilization of alternative, unwanted conformations.

We decided initially to investigate the chemistry of β-amino acids as building blocks for well-defined molecular scaffolding. These offer several advantages including ease of synthesis[11] and the potential for intramolecular hydrogen bonding both to adjacent and distant amide groups.[12] One of the simplest β-amino acids is anthranilic acid. This has the possibility as its diamido derivative to form stable six-membered ring hydrogen bonds between adjacent amides (as in **3**) with the potential of additional binding to the externally directed CO and NH groups. These intramolecular interactions together with the intrinsic rigidity and *trans* preference of the secondary amide bond should, when combined with differently shaped components, provide oligomers with a controllable and stable secondary structure. Moreover, anthranilic acid subunits can be readily prepared with different substituents in the 4- and 5-positions, and their coupling can be accomplished using simple carboxyl activating routes (such as acid chloride, DCC, etc.). The long

[⊗] Abstract published in *Advance ACS Abstracts,* June 15, 1996.

(1) For a recent text, see: Brandon, C.; Tooze, J. *Introduction to Protein Structure*; Garland Publishing Inc.: New York, 1991.

(2) Hassenrück, K.; Murthy, G. S.; Lynch, V.; Michl, J. *J. Org. Chem.* **1990**, *55*, 1013−1016.

(3) Zimmerman, H. E.; Goldman, T. D.; Hirzel, T. K.; Schmidt, S. P. *J. Org. Chem.* **1980**, *45*, 3933−3951.

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(5) For a recent discussion of the role of intramolecular hydrogen bonding in a family of simple diamides, see: Dado, G. P.; Gellman, S. H. *J. Am. Chem. Soc.* **1993**, *115*, 4228−4245.

(6) Several synthetic receptors contain intramolecular hydrogen bonds as an integral part of their structure: Dixon, R. P.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1992**, *114*, 365−367. Nowick, J. S.; Ballester, P.; Ebmeyer, F.; Rebek, J. Jr. *J. Am. Chem. Soc.* **1990**, *112*, 8902−8906. Murray, T. J.; Zimmerman, S. C. *J. Am. Chem. Soc.* **1992**, *114*, 4010−4011.

(7) Nowick, J. S.; Powell, N. A.; Martinez, E. J.; Smith, E. M.; Noronha, G. *J. Org. Chem.* **1992**, *57*, 3763−3765.

(8) Hagihara, M.; Anthony, N. J.; Stout, T. J.; Clardy, J.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 6568−6570.

(9) Cho, C. Y.; Moran, E. J.; Cherry, S. R.; Stephans, J. C.; Fodor, S. P. A.; Adams, C. L.; Sundaram, A.; Jacobs, J. W.; Schultz, P. G. *Science (Washington D.C.)* **1993**, *261*, 1303−1305.

(10) Gennari, C.; Salom, B.; Potenza, D.; Williams, A. **1994**, *3*, 2067−2069. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2067−2069.

(11) Chu, K. S.; Konopelski, J. P. *Tetrahedron* **1993**, 9183−9190, and references therein.

(12) Dado, G. P.; Gellman, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 1054−1062.

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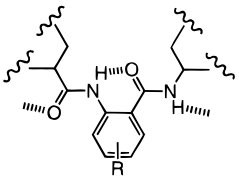

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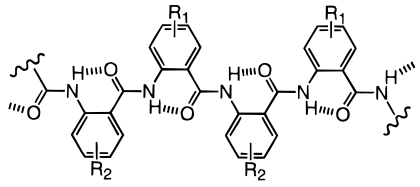

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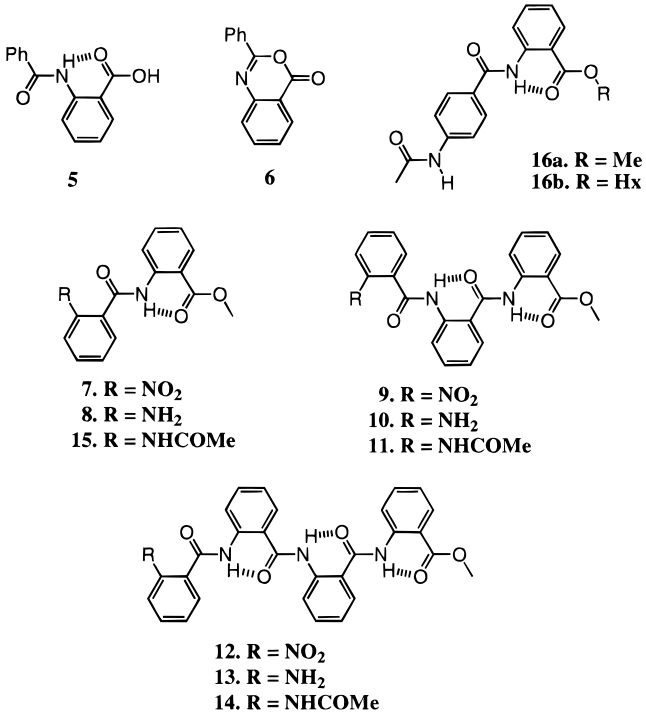
term goal of this work is to develop functionalized molecular scaffolds of defined structure with catalytic or recognition properties. These modular structures can potentially be used in combinatorial synthesis to form a large family of nonpeptide, biopolymer mimetics.[13] In this paper[14] we demonstrate the viability of the approach with the synthesis of two classes of oligomeric anthranilamides which take up, respectively, linear sheet and helical conformations.[15]

The Linear Strand

Simple head-to-tail coupling of anthranilic acid is expected to lead to an oligomer which takes up an extended sheet conformation stabilized, in part, by hydrogen bonding between adjacent amides, as shown in **4**. Initial attempts to effect a stepwise synthesis of these molecules involved carboxyl activation of *N*-benzoylanthranilic acid[16] **5** followed by reaction with aniline derivatives. All activation methods attempted (acid chloride, DCC, CDI, EEDQ) failed to form the anilide product but rather gave azlactone **6**, from intramolecular cyclization of the benzamide oxygen onto the carboxyl derivative.[17] A more successful strategy involved masking the amide as a nitro group which can be reduced to the required amine after amide bond formation.[18,19] Reaction of 2-nitrobenzoyl chloride with methyl anthranilate gave, in 77% yield, nitroamide **7** which could then be hydrogenated over palladized charcoal to amine **8**. Further reaction with 2-nitrobenzoyl chloride gave trimer **9** which was reduced to amine **10**. This could be acetylated with acetyl chloride to trimer **11** or subjected to another sequence of acylation, reduction, and acetylation steps, through **12** and **13**, to tetramer **14**.



5 **6** **16a. R = Me** **16b. R = Hx**

7. R = NO_2 **8. R = NH_2** **15. R = NHCOMe**

9. R = NO_2 **10. R = NH_2** **11. R = NHCOMe**

12. R = NO_2 **13. R = NH_2** **14. R = NHCOMe**

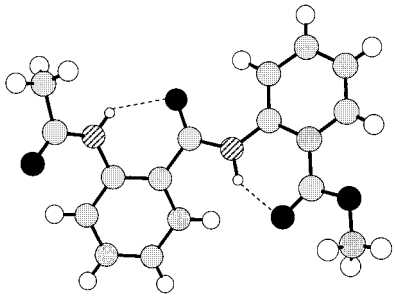


Figure 1. X-ray structure of anthranilamide **15** in extended sheet conformation.

An X-ray structure of the acetylated dimer **15** shows (Figure 1) the expected extended sheet structure with two intramolecular hydrogen bonds between adjacent amide−amide (N···O, 2.75 Å; H···O, 2.06 Å) and amide−ester (N···O, 2.67 Å; H···O, 1.82 Å) groups. The molecule has an almost planar conformation with only a small deviation of the anthranilamide rings from the plane of the amide bonds. Support for this conformation in solution comes from ^{1}H NMR which shows intramolecular NOEs between the amide-NH and the adjacent anthranilamide-6H resonances as well as large downfield shifts of both amide-NH resonances (δ = 12.05 and 11.16 ppm for, respectively, anthranilamide and acetamide in $CDCl_3$).

Similar downfield shifts are seen in the amide-NH resonances of acetylated trimer **11** (δ = 12.24, 12.17, and 11.23 ppm) and tetramer **14** (δ = 12.38, 12.29, 12.19, and 11.23 ppm) in $CDCl_3$. The effect of intramolecular hydrogen bonding on chemical shift is illustrated in control **16a** (formed by a method analogous to **15**) which has a downfield shifted resonance for the hydrogen bonded anthranilamide-NH (12.05 ppm) compared to that of the acetamide (9.94 ppm). Further support for the extended structure in solution comes from variable temperature measurements of the amide-NH resonances. Internally hydrogen bonded amides are expected to show a much smaller shift with temperature ($<3.0 \times 10^{-3}$ ppm K^{-1}) compared to those directed externally and accessible for hydrogen bonding to a polar solvent ($>4.0 \times 10^{-3}$ ppm K^{-1}).[20] Both amide-NH groups in **15** show small changes with temperature in 20% DMSO-d_6/$CDCl_3$ (2.8 and 1.1×10^{-3} ppm K^{-1}) consistent with their involvement in

(13) Liskamp, R. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 633−636.

(14) For preliminary communication of part of this work, see: Hamuro, Y.; Geib, S. J.; Hamilton, A. D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 446−448.

(15) Similar intramolecular hydrogen bonds have been seen in a family of anthranilic acid−amino acid adducts. Feigel, M.; Lugert, G.; Manero, J.; Bremer, M. *Z. Naturforsch.* **1989**, *44b*, 1109−1116. Feigel, M.; Lugert, G.; Manero, J.; Bremer, M. *Z. Natorforsch.* **1990**, *45b*, 258−266.

(16) Steiger, R. E. *J. Org. Chem.* **1944**, *9*, 396−399.

(17) Errede, L. A.; Oien, H. T.; Yarian, D. R. *J. Org. Chem.* **1977**, *42*, 12−18.

(18) A related approach has been used to prepare cyclic anthranilamide oligomers: (a) Hoorfar, A.; Ollis, W. D.; Stoddart, J. F. *Tetrahedron Lett.* **1980**, 4211−4214. (b) Hoofar, A.; Ollis, W. D.; Price, J. A.; Stephanatou, J. S.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans. 1* **1982**, *8*, 1649−1699. (c) Hoofar, A.; Ollis, W. D.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans. 1* **1982**, *8*, 1721−1726. (d) Feigel, M.; Lugert, G.; Manero, J.; Bremer, M. *Liebig Ann. Chem.* **1989**, 1089−1092.

(19) Sengupta, D.; Anand, N. *Indian J. Chem., Sect. B* **1985**, *24B*, 923−927.

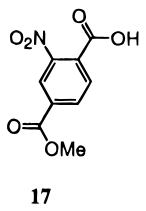
(20) Kessler, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 512−523.

intramolecular hydrogen bonds in solution. In contrast, those of **16a** show both small (anthranilamide; 3.4×10^{-3} ppm K^{-1}) and large (acetamide; 5.8×10^{-3} ppm K^{-1}) temperature effects as would be expected for one internally and one externally directed proton.

IR experiments also support the intramolecular hydrogen bonding secondary structure control in solution. IR spectra of linear strands (**15**, **11**, and **14**), functionalized linear strands (**21**, **23**, and **24**), and helices (**31** and **32**) were taken along with a reference molecule **16b** (2 mM in CH_2Cl_2). For all compounds broad hydrogen bonded N−H stretch peaks were observed around 3200−3300 cm^{-1}, but no peaks were observed in free N−H stretch region (3400−3500 cm^{-1}) except for **16b** which had a relatively sharp peak at 3427 cm^{-1}.[7,12]

Functionalized Linear Strands

This strategy can easily be adapted to allow the incorporation of functionality into the linear strand. The disposition of the substituents along the chain and, in particular, the face from which they project can be controlled by the sequence in which the individual subunits are reacted. For example, 4-(methoxycarbonyl)-2-nitrobenzoic acid **17** could be prepared from the mono esterification (MeOH, H_2SO_4) of 2-nitroterephthalic acid in 64% yield and reacted as its acid chloride with hexyl anthranilate to give the functionalized dimer **18**. Application of the sequential transformations outlined above (including hydrogenation of **18** over palladized charcoal to **19**, reaction with 2-nitrobenzoyl chloride to **20**, further reduction and acylation with 4-(methoxycarbonyl)-2-nitrobenzoyl chloride followed by reduction and acylation with hexanoyl chloride) provided the tetraamide **21**. The methyl esters could be selectively deprotected in 89% yield with LiOH in THF to give the functionalized tetraanthranilamide **22** in which both carboxylic acid groups project from the same face.



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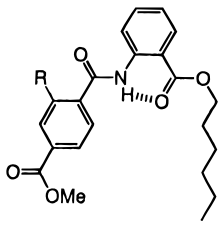
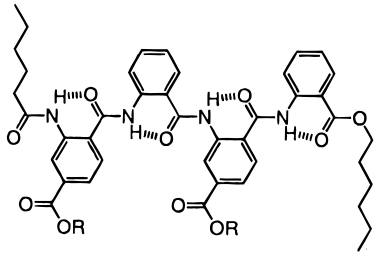


18. R = NO_2
19. R = NH_2



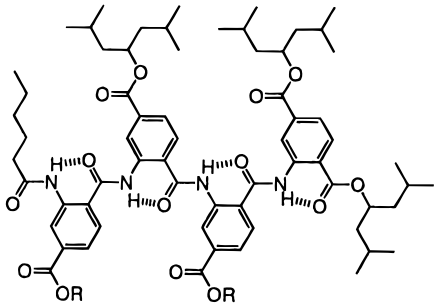
21. R = Me
22. R = H

In a related series of steps differentially protected 2-nitroterephthalic acid derivatives were incorporated into the synthesis in a stepwise manner. The result was a tetramer, **23** or **24**, in which different functionality projected on opposite sides of the linear strand.

Similar downfield shifts of the amide protons, as in simple linear compounds **15**, **11**, and **14**, were observed in functionalized linear compounds **21**−**24** (Table 1). This indicates that intramolecular hydrogen bonding interactions are conserved in these molecules in a similar manner to the simple linear systems.

Table 1. Selected ^{1}H NMR Resonances of linear Oligoanthranilamides

		chemical shifts (ppm)			
compd	solvent	acylamide NH	anthranilamide NH's		
15	$CDCl_3$	11.16	12.05		
15	DMSO-d_6	10.42	11.29		
16a	$CDCl_3$	9.94	12.05		
11	$CDCl_3$	11.23	12.17	12.24	
14	$CDCl_3$	11.23	12.19	12.29	12.38
21	$CDCl_3$	11.11	12.32	12.38	12.38
22	DMSO-d_6	10.35	11.27	11.37	11.41
23	$CDCl_3$	11.15	12.26	12.44	12.44
24	$CDCl_3$	11.44	12.57	12.83	12.93

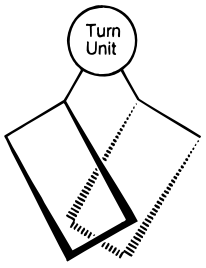


23. R = Me
24. R = H

The conservation of this conformation in solution suggests the potential application of this series of molecules as scaffolds.

The Turn

Further development of the anthranilamides as general scaffolding subunits required a family of components that would enforce a turn in the molecule and so lead to potentially helical conformations, as in **25**. Several spacers can be envisioned that would provide a turn unit through which two linear strands can



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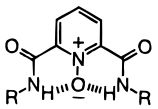
be attached. Because a key goal of this work is to maintain structure by intramolecular hydrogen bonding, an interesting candidate was pyridine-2,6-dicarboxamide *N*-oxide **26** and its derivatives. A crystal structure of the corresponding dicarboxylic acid[21] **27** shows two very short, six-membered ring intramolecular hydrogen bonds between the acidic hydrogens and the *N*-oxide (O···O; 2.48 and 2.45 Å). Analogous interactions would be expected to stabilize a turn between two anthranilamide units (where R = 2-benzoate) with an approximately 120° angle between the phenyl-N bonds. Furthermore,

(21) For a crystal structure, see: (a) Rychlewska, U.; Gdaniec, M. *Acta Cryst.* **1977**, *B33*, 3555−3558. (b) Brzezinski, B.; Zundel, G.; Krämer, R. *Chem. Phys. Lett.* **1986**, *124*, 395−400. For a synthesis, see: (c) Heywood, D.; Dunn, J. *J. Org. Chem.* **1959**, *24*, 1569−1570.



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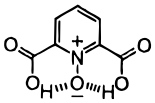

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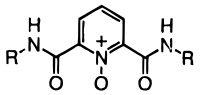

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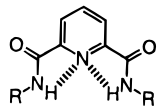
this arrangement would be favored by a destabilization of the alternative planar conformation **28** in which three electronegative oxygen atoms are in close proximity. A simple modification of the approach would involve using pyridine-2,6-dicarboxamide **29** in place of the *N*-oxide. Several X-ray structures of pyridine-2-carboxamide or pyridine-2,6-dicarboxamide derivatives[22] show an almost planar arrangement of the pyridine and carboxamide groups with close positioning of the pyridine-N and amide-H (N···N, 2.73 and 2.74 Å, N···H, 2.61 and 2.63 Å), consistent with formation of two weak hydrogen bonds (as in **29**).



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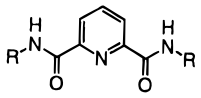

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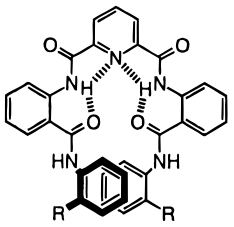
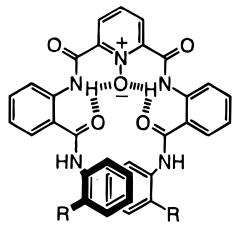
However, intramolecular hydrogen bonding may play a minor role in **29** due to the reduced basicity of the pyridine and the less favorable five-membered ring.[23] As with **28** the repulsive electrostatic interactions present in the alternative conformation **30** (from 180° rotation of each pyridine−carboxamide bond) should also lead to an increased population of the desired turn structure **29**. This is further supported by recent computational studies on pyridine-2,6-dicarboxamide derivatives which show a preference of conformation **29** over **30** by 112 kcal mol^{-1} in the gas phase.[24] The five- or six-membered ring intramolecular hydrogen bonding arrangements in **26** or **29** should allow a manipulation of the relative orientations of the two anthranilamide subunits.

The Helix

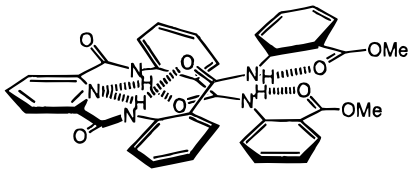
Combining the strand and turn subunits discussed above can lead in a very simple way to structures with a helical conformation stabilized by a network of intramolecular hydrogen bonds between the different components. For example, reaction of amine **8** with pyridine-2,6-dicarbonyl chloride or pyridine-*N*-oxide-2,6-dicarbonyl chloride gave tetraamides **31** and **32** in 76% and 69% yield, respectively.[25] In both **31** and **32** the key structural features that will determine the preferred conformation are the intramolecular hydrogen bonds, the rigidity and *trans* requirement of the amide bonds, and the destabilization of alternative conformations. These all should constrain the molecule into a geometry that positions the two terminal anthranilamide rings above and below each other. The resulting helical structure (shown from the side in **33**) can be compared to the structure of the helicenes,[26] but in this case stabilization derives from hydrogen bonding rather than fused aromatic rings.[27−29] A second series of molecules was formed from the reaction of the anilide of anthranilic acid with the two pyridine diacid chlorides to give **36** and **37**.



31. R = COOMe
36. R = H



32. R = COOMe
37. R = H



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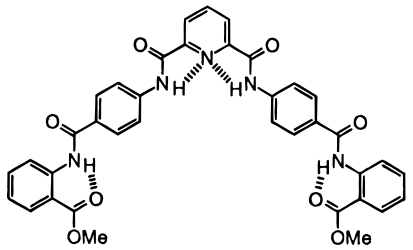

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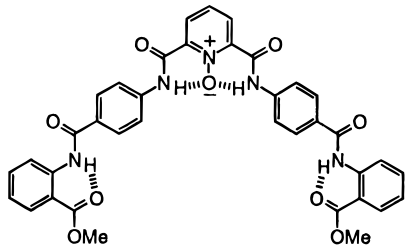

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The X-ray crystal structures of **31** and **32** have been determined and confirm that both molecules take up a helical conformation in the solid state. The structure of **31** shows (Figure 2) a clear helical arrangement of the five rings stabilized by a network of intramolecular hydrogen bonds (NH_a···N, 2.20 and 2.21 Å; NH_a···OC, 1.82 and 2.02 Å; NH_b···OC, 1.92 and 1.88 Å). As expected, the distance between the pyridine-N atom

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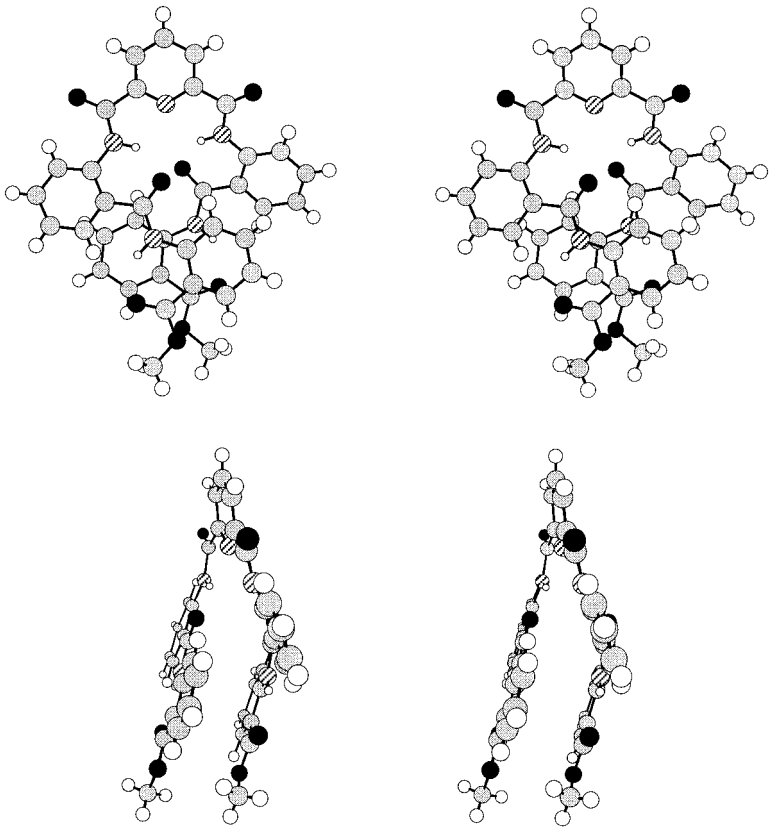

Figure 2. Stereo representations of the front and side view of the X-ray structure of helical oligoanthranilamide **31**.

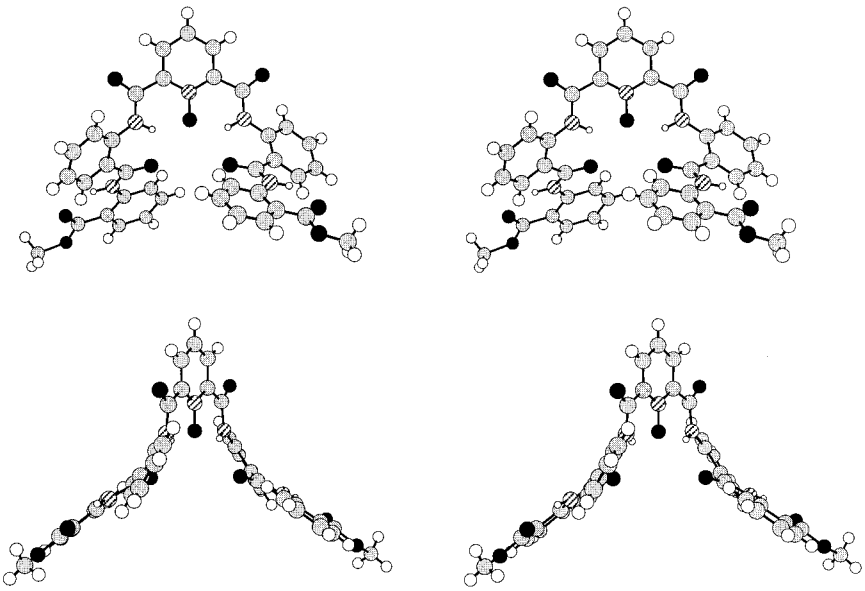

Figure 3. Stereo representations of the front and side view of the X-ray structure of helical oligoanthranilamide **32**.

and the adjacent amide-NH is relatively long reflecting the poor hydrogen bond accepting character of the heterocycle. The molecule forms a tight coil with close contact between the terminal anthranilamide rings and a distance of 5.41 Å from one center of the ring to the other, representing a helix with a relatively small pitch. As a consequence of this conformation the protons in the 4- and 5-position of the terminal phenyl ring are positioned close to the face of the first anthranilamide ring (Ph_a). Figure 2 shows the right-handed helix; however, the crystal is racemic with both right- and left-handed forms present in the unit cell.

The X-ray structure of **32** (Figure 3) shows the persistence of the helical motif despite changes in the molecule. The network of hydrogen bonds in the turn region is apparent although in this case the more favored six-membered ring hydrogen bonding to the *N*-oxide leads to a shortening of the H-bonding distance to the pyridine carboxamide-NH ($NH_a\cdots$ ON, 1.83 and 1.84 Å) and a lengthening of the first anthranilamide interaction ($NH_a\cdots$OC, 2.12 and 2.14 Å), with two further hydrogen bonds ($NH_b\cdots$OC, both 1.88 Å) in the terminal anthranilamide rings. In addition, there is a wider separation (compared to **31**) of the two terminal anthranilamide rings (the distance of two centers of the rings, 10.91 Å in **32**). The resultant increase in the pitch of the helix is presumably due to the greater steric bulk of the pyridine *N*-oxide in the turn region as well as the formation six- (rather than five-) membered ring

Table 2. Selected ^{1}H NMR Resonances of Oligoanthranilamides in 20% DMSO−d_6/80% $CDCl_3$[a]

compd	concn (mM)	NH_a	NH_b	Ph_a6	Ph_a5	Ph_a4	Ph_a3	Ph_b6	Ph_b5	Ph_b4	Ph_b3
15	2	11.08	12.02	7.88	7.23	7.54	8.58	8.12	7.21	7.66	8.76
16a	2	9.94	11.99	7.79	7.79	7.96	7.96	8.10	7.14	7.60	8.87
31	10	13.05	11.61	7.57	7.25	7.65	8.85	7.92	6.92	6.69	8.45
32	2	13.68	11.77	7.86	7.37	7.66	8.58	7.92	6.95	7.29	8.81
34	saturtd	12.10	11.21	8.13	8.13	8.24	8.24	8.13	7.17	7.63	8.54
35	2	12.58	12.24	7.99	7.99	8.36	8.36	8.13	7.25	7.35	8.80
36	10	12.48	9.74	7.78	7.27	7.55	8.38	6.89	6.89	6.89	7.29
37	10	13.15	10.08	7.73	7.31	7.54	8.23	7.17	6.97	7.17	7.73

[a] Ph_a and NH_a refer to those groups adjacent to the pyridine and Ph_b and NH_b to the terminal anthranilate.

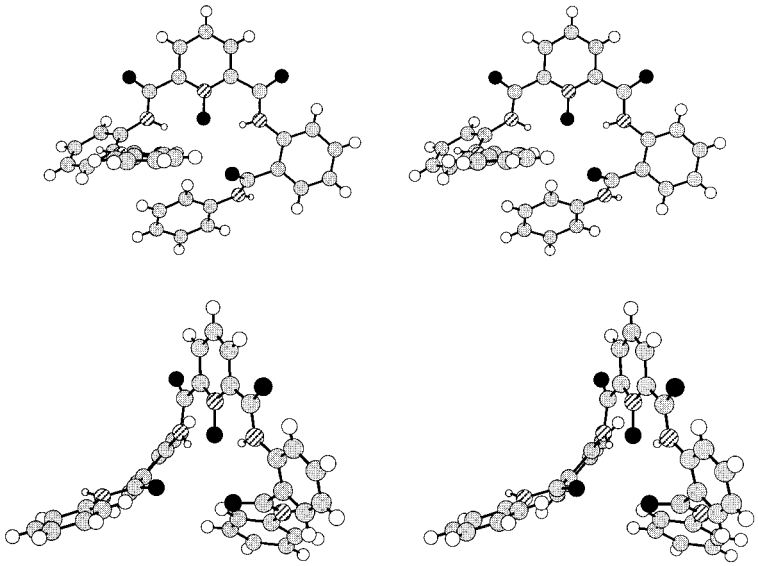

Figure 4. Stereo representations of the front and side view of the X-ray structure of helical oligoanthranilamide **37**.

intramolecular hydrogen bonds. This simple expansion in the helical structure offers potential in the future for subtle modification of the folded structures.

The key question of whether these helical conformations are maintained in solution can be investigated by ^{1}H NMR and by comparisons to controls such as **34** which due to the *para* relationship of the substituents is incapable of forming a helix. The spectrum of **31** in 20% DMSO-d_6/80% $CDCl_3$ solution shows several features consistent with a helical structure, and some of these resonances are collected with those of other oligomers in Table 2. In particular, there is a large downfield shift of the pyridine carboxamide-NH_a resonance in **31** compared to the equivalent resonance in **15** and **34** indicating a bifurcated intramolecular hydrogen bond from the first anthranilamide-NH_a to both pyridine-N and carbonyl-O. In contrast, the second amide-NH_b as well as the 6-, 5-, 4-, and 3-protons of the terminal anthranilamide are shifted upfield (0.41, 0.20, 0.29, 0.97, and 0.31 ppm, respectively) compared to **15**. This is consistent with their position in a helical conformation above the ring current of the opposing aromatic rings, as depicted in **33**. The nearly 1 ppm upfield shift of the proton in the 4-position of the terminal ring appears to correlate well with the crystal structure of **31** which shows it positioned directly above the plane of the first anthranilamide ring. The ^{1}H NMR spectrum of **32** in 20% DMSO-d_6/80% $CDCl_3$ is similar to that of **31** with large downfield shifts of the amide-NH_a and NH_b resonances, reflecting strong intramolecular hydrogen bonding in solution. However, the expanded helical structure of **32** which is seen in the crystal (Figure 3) is also suggested by its ^{1}H NMR spectrum which shows (Table 2) smaller upfield shifts of Ph_b-4H and Ph_b-5H due to the greater distance between the aromatic rings.

Further support for the role of intramolecular hydrogen bonding in stabilizing the helical conformation of **31** comes from the temperature dependence of the amide-NH resonances in 20% DMSO-d_6/$CDCl_3$. Both NH_a and NH_b in **31** show a small variation with temperature (2.9×10^{-3} and 1.1×10^{-3} ppm K^{-1}, respectively), as expected for intramolecularly H-bonded amide-NH groups in a polar solvent.[13] As a comparison, the anilide-NH in **36**, which is incapable of intramolecular H-bonding, shows a large upfield shift with increasing temperature (7.5×10^{-3} ppm K^{-1}), while the NH_a resonance undergoes little change (2.1×10^{-3} ppm K^{-1}).

This helical motif based on the pyridine and pyridine-*N*-oxide turn region appears to be a general one. Removing the carboxyl substituent in the terminal rings,[30] as in anilides **36** and **37**, leads to a loss of the structural control imposed by the intramolecular hydrogen bond and a consequent increase in flexibility around the phenyl-N bond. Nonetheless, in both molecules the helical conformation is maintained. The X-ray structure of *N*-oxide **37** shows a helical arrangement of the six-membered rings stabilized by two short (NO···HN, 1.82 and 1.86 Å) and two long (NH···OC, 2.42 and 2.21 Å) intramolecular hydrogen bonds (Figure 4). The overall structure is similar to that of **32** with an expanded helix and a terminal ring distance of 8.65 Å. The major disruption compared to **32** is the requirement for the anilide-NH to satisfy its hydrogen bonding needs intermolecularly rather than intramolecularly. Each helix forms two intermolecular hydrogen bonds to a neighboring helix of opposite handedness (from the anilide-NH to the pyridine-CO and visa versa). In pyridine **36** the formation of extensive

(30) For the synthesis of anthranylaniline, see: Clark, C. R.; Lin, C. M.; Sansom, R. T. *J. Med. Chem.* **1986**, *29*, 1534−1537.

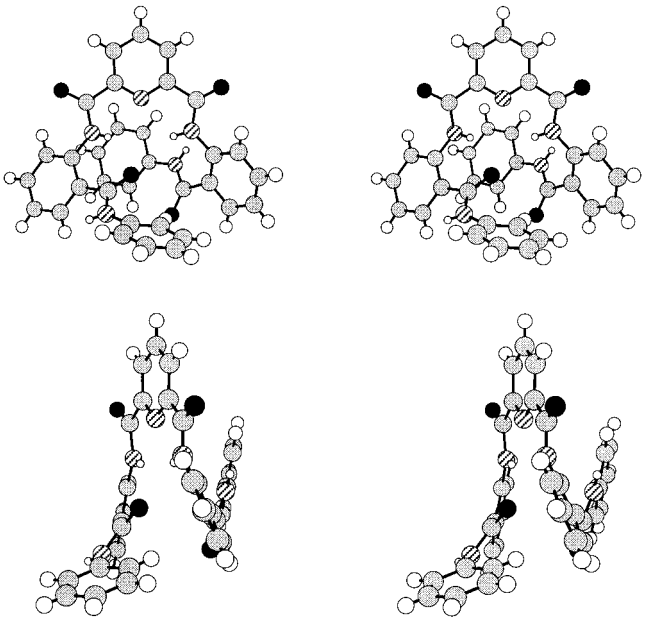

Figure 5. Stereo representation of the front and side view of the X-ray structure of helical oligoanthranilamide **36**.

Table 3. ^{1}H NMR Variable Temperature Data (from −40 to 40 °C in 20% DMSO-d_6/80% $CDCl_3$)

compd	concn (mM)	NH_a (10^{-3} ppm K^{-1})	NH_b (10^{-3} ppm K^{-1})
15	2	−1.1	−2.8
16a	2	−5.8	−3.4
31	10	−2.9	−1.1
32	2	−4.0	−3.4
36	10	−2.1	−7.5
37	10	−3.0	−6.6

Table 4. X-ray Crystal Structure Data

compd	NO···H_aN or N···H_aN	NH_a···OC	NH_b···OC	distance of two rings[a]	solvent system for recrystallization
15		2.06	1.82		AcOEt/hexane
31	2.21	2.02	1.88	5.41	$CHCl_3$/hexane
	2.20	1.82	1.92		
32	1.83	2.12	1.88	10.91	THF/hexane
	1.84	2.14	1.88		
36	2.20	3.71		8.32	DMSO/THF/Et_2O
	2.25	2.11			
37	1.82	2.42		8.65	THF/hexane
	1.86	2.21			

[a] Distance between two terminal rings, the average of the distance of two Ph_b2C's and that of Ph_b5C's.

intermolecular contacts causes a larger deviation of the structure from that in **31** (Figure 5). Each arm of each helix forms two intermolecular hydrogen bonds to a neighboring helix analogous to those in **37**. In addition one anilide in Figure 5 forms an edge-to-face interaction with the terminal anilide of second helix. Despite a disruption of the π-stacking in the terminal rings (terminal ring distance, 8.32 Å) and the formation of an unexpected face-to-face π-stacking (the distance between the terminal ring of the right arm and the anthranilamide ring of the left arm, 4.34 Å), the pyridine-2,6-dicarboxamide imposes a helical conformation on the molecule (NH_a···N, 2.20 and 2.25 Å; NH_a···OC, 3.71 and 2.11 Å).

In summary, we have shown that a very simple series of anthranilic acid based subunits can be induced to take up, in both the solution and solid state, linear and helical secondary structural features stabilized, in part, by intramolecular hydrogen bonds. These conformational features are quite general and are taken up despite introduction of significant substitution or other structural changes into the molecules. We are currently preparing extended and substituted versions of these scaffolds to act as structural and functional analogs of protein secondary structures.

Experimental Section

General Methods. CH_2Cl_2 was obtained from Fisher and distilled from P_2O_5. Et_2O and THF were obtained from Fisher and distilled from sodium benzophenone ketyl. All other reagents, unless otherwise noted, were obtained from the Aldrich Chemical Company and used without further purification.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-300 (300 MHz). NMR chemical shifts are reported in ppm downfield from internal TMS. FT-IR spectra were obtained on Mattson Cygnus 100 instrument. CaF_2 IR cell having a path length of 1.0 mm was used. Mass spectra were determined at the Department of Chemistry, University of Pittsburgh. EI and FAB mass spectra (MS) were obtained using a Varian MAT CH-5 or VG 7070 mass spectrometer under the direction of Dr. Kasi V. Somayajula. Melting points were determined using an Electrothermal capillary melting point apparatus and are uncorrected. Elemental analysis was carried out by Atlantic Microlab, Inc., Norcross, GA.

Analytical thin layer chromatography (TLC) was conducted using PolyGram 0.25 mm silica gel precoated plates with fluorescent indicator UV_{254}. Silica gel 60 (particle size 0.063−0.200 mm, 70−230 mesh ASTM) (EM Science) was used for flash chromatography.

2-Benzoylaminobenzoic Acid (5). This compound was synthesized according to a literature procedure:[16] mp 180−181 °C (lit.[16] 181−182 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.82 (s, 1H, acid), 12.19 (s, 1H, amide), 8.71 (d, J = 8.7 Hz, 1H), 8.05 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 7.2 Hz, 2H), 7.62 (m, 4H), 7.20 (t, J = 7.7 Hz, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 170.1, 164.7, 141.2, 134.5, 134.4, 132.2, 131.3, 129.0, 127.0, 123.0, 119.9, 116.5; HRMS *m*/*e* calcd for $C_{14}H_{11}NO_3$ 241.0728, found 241.0739. Anal. calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.75; H, 4.65; N, 5.79.

2-Phenyl-4*H*-3,1-benzoxazin-4-one (6). A solution of **5** (121 mg, 0.50 mmol) and oxalyl chloride (72 mg, 0.55 mmol) in dry CH_2Cl_2 (3 mL) was stirred and cooled in an dry-ice/acetone bath. DMF (0.025 mL) was added to the mixture which was then stirred in an ice bath for 3 h. Aniline (140 mg, 1.50 mmol) was added to the reaction mixture which was then stirred for 10 min in the ice bath. After adding CH_2Cl_2 (15 mL), the reaction mixture was washed with 1 N HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), and H_2O (15 mL). The organic layer was evaporated in vacuo to obtain a white powder. This white powder seemed to be a cyclized compound from the results of NMR and MS. The same compound was observed when BOP-Cl was used for the same coupling reaction: mp 118−119 °C (lit.[17] 122−123 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, J = 7.8 Hz, 2H), 8.25 (d, J = 7.8 Hz, 1H), 7.84 (t, J = 7.7 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.55 (m, 4H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 157.1, 147.0, 136.6, 132.6, 130.2, 128.8, 128.6, 128.33, 128.28, 127.3, 119.9, 117.0; HRMS *m*/*e* calcd for $C_{14}H_9N_2O$ 223.0633, found 223.0631.

2-(2-Nitrobenzoylamino)benzoic Acid Methyl Ester (7). A solution of 2-nitrobenzoic acid (33.4 g, 200 mmol) and oxalyl chloride (27.9 g, 220 mmol) in dry CH_2Cl_2 (200 mL) was stirred and cooled in an ice bath. DMF (0.78 g, 22 mmol) was added dropwise through a silica gel filter, and the mixture was stirred at room temperature for 4 h. The reaction mixture was evaporated in vacuo to obtain the acid chloride as a yellow oil. A solution of methyl anthranilate (30.2 g, 200 mmol) and pyridine (16.6 g, 220 mmol) in dry CH_2Cl_2 (200 mL) was cooled in an ice bath with stirring. A solution of 2-nitrobenzoyl chloride in CH_2Cl_2 (150 mL) was added dropwise for 15 min to the reaction mixture, and then pyridine (11.0 g) was added to the mixture. The mixture was stirred at room temperature for an additional 1 h. CH_2Cl_2 (400 mL) was added to the mixture which was then washed with 1 N HCl (500 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give crude product (55.3 g, 92%). The crude product was recrystallized from AcOEt (450 mL) and hexane (500 mL) to obtain the desired compound as a pale yellow powder (46.4 g, 77%): mp 158−160 °C (lit.[19] 146−147 °C); ^{1}H NMR (300 MHz,

$CDCl_3$) δ 11.55 (s, 1H, amide), 8.82 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.70 (m, 4H), 7.18 (t, J = 7.7 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.7, 164.4, 146.9, 141.0, 134.8, 133.8, 132.9, 130.9, 128.2, 124.7, 123.4, 120.6, 115.3, 52.5; HRMS *m/e* calcd for $C_{15}H_{12}N_2O_5$ 300.0746, found 300.0742. Anal. calcd for $C_{15}H_{12}N_2O_5$: C, 60.00; H, 4.03; N, 9.33. Found: C, 60.09; H, 4.04; N, 9.36.

2-(2-Aminobenzoylamino)benzoic Acid Methyl Ester (8). A solution of **7** (3.85 g, 12.8 mmol) and 10% Pd/C (0.39 g) in DMF (45 mL) was prepared in a 250-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously for 15 h at room temperature. The catalyst was removed by filtration through Celite. CH_2Cl_2 (300 mL) was added to the filtrate which was then washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic layers were dried over $MgSO_4$ and evaporated in vacuo to give the desired compound as a red solid (3.34 g, 96%). This compound was used without further purification in the next step: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.83 (s, 1H, amide), 8.82 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.26 (t, J = 8.1 Hz, 1H), 7.10 (t, J = 7.7 Hz, 1H), 6.78 (t, J = 7.7 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 5.75 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 168.2, 149.6, 141.9, 134.6, 132.6, 131.0, 127.7, 122.4, 120.4, 117.7, 117.1, 115.8, 115.3, 52.5.

2-(2-(2-Nitrobenzoylamino)benzoylamino)benzoic Acid Methyl Ester (9). The nitro trimer **9** was prepared by a method analogous to the dimer **7**. A solution of the acid chloride from 2-nitrobenzoic acid (10.0 g, 60 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a solution of **8** (8.11 g, 30 mmol) and pyridine (55.8 g, 60 mmol) in DMF (100 mL) and CH_2Cl_2 (100 mL). The crude product was recrystallized from AcOEt and hexane three times to obtain the desired compound as pale yellow thin needles (4.68 g, 37%): mp 156−158 °C (lit.[18c] 155 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.14 (s, 1H, amide), 11.74 (s, 1H, amide), 8.82 (d, J = 8.4 Hz, 1H), 8.67 (d, J = 8.4 Hz, 1H), 8.09 (t, J = 6.8 Hz, 2H), 7.94 (d, J = 8.1 Hz, 1H), 7.73 (m, 2H), 7.63 (m, 3H), 7.31 (t, 1H), 7.16 (t, 1H), 3.98 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 167.8, 164.4, 147.1, 140.9, 140.1, 134.7, 133.8, 133.5, 133.2, 131.2, 130.8, 128.5, 127.3, 124.8, 124.1, 123.4, 122.0, 120.7 (2), 115.9, 52.8; HRMS *m/e* calcd for $C_{22}H_{17}N_3O_6$ 419.1088, found 419.1117. Anal. calcd for $C_{22}H_{17}N_3O_6$: C, 63.01; H, 4.09; N, 10.02. Found: C, 63.13; H, 4.09; N, 10.00.

2-(2-(2-Aminobenzoylamino)benzoylamino)benzoic Acid Methyl Ester (10). The amine **10** was prepared by a route analogous to **8** using **9** (3.15 g, 7.5 mmol) and 10% Pd/C (0.32 g) in DMF (30 mL). The crude product was a mixture of DMF and the desired compound (3:4 mol ratio), indicating the purity of this product was 88% (weight) and the yield of this reaction was 91%. The material was used without further purification in the next step: ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.08 (s, 1H, amide), 11.95 (s, 1H, amide), 8.84 (d, J = 8.4 Hz, 1H), 8.74 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.60 (m, 2H), 7.24 (t, 1H), 7.16 (t, 1H), 6.75 (t, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.76 (s, 2H), 3.96 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 168.1, 168.0, 149.8, 141.1, 140.7, 134.8, 133.0, 132.8, 131.1, 127.9, 127.3, 123.2, 123.1, 121.8, 121.0, 120.7, 117.5, 117.0, 115.8, 115.6, 52.7; HRMS *m/e* calcd for $C_{22}H_{19}N_3O_4$ 389.1376, found 389.1418.

2-(2-(2-Acetylaminobenzoylamino)benzoylamino)benzoic Acid Methyl Ester (11). To a solution of **10** (389 mg, 1 mmol) and pyridine (372 mg, 4.0 mmol) in DMF (4 mL) was added acetyl chloride (314 mg, 4.0 mmol) dropwise, and then the mixture was stirred at room temperature for 3 h. CH_2Cl_2 (40 mL) was added to the reaction mixture which was then washed with 1 N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give crude product as a pale yellow solid (363 mg). The crude product was recrystallized from THF (50 mL) and hexane (60 mL) to obtain the desired compound as a white powder (306 mg, 71%): mp 233−235 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.24 (s, 1H, anthranilamide), 12.17 (s, 1H, anthranilamide), 11.23 (s, 1H, acetamide), 8.81 (d, J = 8.4 Hz, 1H), 8.72 (d, J = 9.3 Hz, 2H), 8.10 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 6.6 Hz, 1H), 7.63 (m, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.19 (m, 2H), 3.97 (s, 3H, 2.23 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1 (2), 167.9 (2), 141.1, 140.4, 139.9, 134.9, 133.2, 133.1, 131.2, 127.4, 127.3, 124.1, 123.5, 123.2 (2), 122.0, 121.4, 120.8, 120.5, 115.8; IR (2 mM in CH_2Cl_2) 3270, 1695, 1660, 1586, 1521 cm^{-1}; HRMS *m/e* calcd for $C_{24}H_{21}N_3O_5$ 431.1481, found 431.1463. Anal. calcd for $C_{24}H_{21}N_3O_5$: C, 66.81; H, 4.91; N, 9.78. Found: C, 66.77; H, 4.91; N, 9.76.

2-(2-(2-(2-Nitrobenzoylamino)benzoylamino)benzoylamino)benzoic Acid Methyl Ester (12). To a solution of **10** (2.14 g, 5.5 mmol) and pyridine (2.05 g, 22 mmol) in DMF (22 mL) was added 2-nitrobenzoyl chloride (4.08 g, 22 mmol), and then the reaction mixture was stirred at room temperature for an additional 2 h. CH_2Cl_2 (200 mL) was added to the mixture which was then washed with 1 N HCl (100 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give the crude product as an orange solid (3.56 g). The crude product was recrystallized from AcOEt (600 mL) and hexane (300 mL) to obtain the desired compound as a pale brown powder (746 mg, 25%): mp 234−235 °C (lit.[18c] 226−228 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.34 (s, 1H, anthranilamide), 12.17 (s, 1H, anthranilamide), 11.89 (s, 1H, acetamide), 8.83 (m, 2H), 8.60 (d, J = 8.1 Hz, 1H), 8.09 (m, 2H), 7.96 (d, J = 6.8 Hz, 2H), 7.72 (m, 2H), 7.62 (m, 4H), 7.29 (m, 2H), 7.19 (t, 1H), 3.97 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 167.9, 167.7, 164.4, 147.0, 141.0, 140.2, 139.8, 134.9, 133.8, 133.4, 133.3, 133.2, 131.2, 130.8, 128.6, 127.5 (2), 124.8, 124.2 (2), 123.6, 122.1, 121.9, 121.6, 120.9, 120.7, 115.8, 52.8; HRMS *m/e* calcd for $C_{29}H_{22}N_4O_7$ 538.1488 found 538.1468. Anal. calcd for $C_{29}H_{22}N_4O_7$: C, 64.68; H, 4.12; N, 10.40. Found: C, 64.56; H, 4.14; N, 10.37.

2-(2-(2-(2-Aminobenzoylamino)benzoylamino)benzoylamino)benzoic Acid Methyl Ester (13). A suspension of the aforementioned nitro compound **12** (539 mg, 1.0 mmol) and 10% Pd/C (108 mg) in DMF (20 mL) was prepared in a 100 mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator and the solution was stirred vigorously for 2 h at room temperature. The reaction mixture was filtered through a glass filter. CH_2Cl_2 (160 mL) was added to the filtrate which was then washed with brine (50 mL). CH_2Cl_2 (100 mL) and DMF (40 mL) were added to the filtered residue which was then washed with brine (50 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated in vacuo to obtain the title compound as a yellow solid (522 mg). The NMR indicated that this product was the mixture of DMF and the desired compound (1:1 mol ratio). This means the purity of this product was 87% (weight), and the yield of this reaction was 90%: ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.28 (s, 1H, amide), 12.16 (s, 1H, amide), 12.01 (s, 1H, amide), 8.76 (m, 3H), 8.11 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 7.8 Hz, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.62 (m, 3H), 7.26 (m, 5H), 6.78 (t, J = 7.7 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.76 (s, 2H), 3.97 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 168.1, 168.0 (2), 149.3, 141.0, 140.6, 140.0, 134.9, 133.3, 133.0, 132.8, 131.2, 128.0, 127.5, 127.4, 124.0, 123.5, 123.3, 122.2, 121.8, 121.4, 120.9 (2), 117.7, 117.4, 116.0, 115.8, 52.8.

2-(2-(2-(2-Acetylaminobenzoylamino)benzoylamino)benzoylamino)benzoic Acid Methyl Ester (14). The tetramer **14** was prepared by a route analogous to trimer **11** using aforementioned amine **13** (261 mg, 0.50 mmol), pyridine (1400 mg, 15 mmol), and acetyl chloride (1200 mg, 15 mmol). The crude product (397 mg) was recrystallized from AcOEt (130 mL) and hexane (120 mL) to obtain the desired compound as a pale brown powder (142 mg, 50%): mp 235−236 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.38 (s, 1H, amide), 12.29 (s, 1H, amide), 12.19 (s, 1H, amide), 11.23 (s, 1H, amide), 8.82 (d, J = 8.7 Hz, 1H), 8.71 (m, 2H), 8.11 (d, J = 8.1 Hz, 1H), 7.98 (t, J = 7.7 Hz, 3H), 7.90 (d, J = 8.1 Hz, 1H), 7.62 (m, 3H), 7.52 (t, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.22 (m, 2H), 3.97 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 168.0, 167.86, 167.82, 167.77, 141.1, 140.4, 139.94, 139.88, 134.9, 133.3, 133.0 (2), 131.2, 127.7, 127.4 (2), 124.2, 124.1, 123.5, 123.2, 122.2, 121.9, 121.5, 121.4, 121.3, 120.8, 120.6, 115.9, 52.8, 25.5; IR (2 mM in CH_2Cl_2) 3260, 1694, 1655, 1608, 1588, 1516 cm^{-1}; HRMS *m/e* calcd for $C_{31}H_{26}N_4O_6$ 550.1852, found 550.1852.

2-(2-Acetylaminobenzoylamino)benzoic Acid Methyl Ester (15). The dimer **15** was synthesized by a route analogous to trimer **11** using amine **9** (2.70 g, 10 mmol), pyridine (1.86 g, 20 mmol) and acetyl chloride (1.57 g, 20 mmol). The crude product (3.12 g) was

recrystallized from AcOEt (100 mL) and hexane (150 mL) to obtain the desired compound as pink crystals (2.72 g, 87%): mp 185−187 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.05 (s, 1H, anthranilamide), 11.16 (s, 1H, acetamide), 8.77 (d, J = 8.4 Hz, 1H), 8.67 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.53 (t, J = 7.9 Hz, 1H), 7.20 (m, 2H), 3.96 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.9, 168.8, 167.7, 141.0, 140.3, 134.8, 133.0, 131.0, 127.0, 123.1, 123.0, 121.4, 120.4, 120.2, 115.6, 52.6, 25.4; IR (2 mM in CH_2Cl_2) 3260, 1694, 1653, 1608, 1584, 1512 cm^{-1}; HRMS *m*/*e* calcd for $C_{16}H_{16}N_2O_4$ 312.1087, found 312.1110. Anal. calcd for $C_{16}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.28; H, 5.21; N, 8.90.

2-(4-Nitrobenzoylamino)benzoic Acid Methyl Ester. This nitro compound was prepared by a route analogous to **7** using 4-nitrobenzoic acid (16.7 g, 100 mmol), oxalyl chloride (14.0 g, 110 mmol), methyl anthranilate (15.1 g, 100 mmol), and pyridine (8.71 g, 110 mmol). The crude product (27.3 g) was recrystallized from THF (950 mL) and hexane (350 mL) to obtain the desired compound as pale yellow needles (24.9 g, 83%): mp 197−199 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.56 (s, 1H, amide), 8.42 (m, 3H), 8.18 (d, J = 8.7 Hz, 2H), 7.99 (d, J = 8.1 Hz, 1H), 7.70 (t, J = 7.7 Hz, 1H), 3.87 (s, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 167.8, 149.5, 140.0, 139.2, 134.2, 130.7, 128.8, 124.3, 124.2, 121.8, 118.8, 52.7; HRMS *m*/*e* calcd for $C_{15}H_{12}N_2O_5$ 300.0727, found 300.0746. Anal. calcd for $C_{15}H_{12}N_2O_5$: C, 60.00; H, 4.03; N, 9.33. Found: C, 60.10; H, 4.04; N, 9.31.

2-(4-Aminobenzoylamino)benzoic Acid Methyl Ester. A solution of 2-(4-nitrobenzoylamino)benzoic acid methyl ester (3.0 g, 10.0 mmol) and 10% Pd/C (0.30 mg) in DMF (15 mL) was prepared in a 50-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously overnight at room temperature. The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give desired compound as pale brown crystals (2.62 g, 97%). This compound was used without further purification in the next step: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.47 (s, 1H, amide), 8.66 (d, J = 8.1 Hz, 1H), 8.01 (dd, J = 7.8, 1.5 Hz, 1H), 7.65 (m, 3H), 7.15 (d, J = 7.2 Hz, 1H), 6.64 (d, J = 8.7 Hz, 2H), 5.92 (s, 2H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 168.3, 164.6, 152.8, 141.6, 134.4, 130.7, 128.8, 122.1, 120.4, 119.9, 115.2, 113.0, 52.5.

2-(4-Acetylaminobenzoylamino)benzoic Acid Methyl Ester (16a). To a solution of 2-(4-aminobenzoylamino)benzoic acid methyl ester (512 mg, 2.0 mmol) and pyridine (280 mg, 6.0 mmol) in dry THF (10 mL) was added acetyl chloride (236 mg, 6.0 mmol), and the mixture was stirred at room temperature for 40 min. Hexane (50 mL) was added to the mixture, and the precipitate was collected on a glass filter. The filtered residue was washed wtih 1 N HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and H_2O (2 × 30 mL) on the filter. The crude product was recrystallized from THF (150 mL) and hexane (150 mL) to obtain the desired compound as white crystals (512 mg, 82%): mp 252−253 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.54 (s, 1H, benzamide), 10.29 (s, 1H, acetamide), 8.57 (d, J = 8.7 Hz, 1H), 8.01 (dd, J = 7.8, 1.4 Hz, 1H), 7.90 (d, J = 8.7 Hz, 2H), 7.77 (d, J = 8.7 Hz, 2H), 7.67 (td, J = 8.0, 1.5 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 3.89 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 168.9, 168.1, 164.2, 142.9, 140.5, 134.4, 130.7, 128.4, 128.1, 123.1, 120.6, 118.6, 116.7, 52.7, 24.2; HRMS *m*/*e* calcd for $C_{17}H_{16}N_2O_4$ 312.1110, found 312.1118. Anal. calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.46; H, 5.20; N, 8.90.

2-(4-Acetylaminobenzoylamino)benzoic Acid Hexyl Ester (16b). A solution of 4-acetamidobenzoic acid (358 mg, 2.0 mmol) and oxalyl chloride (508 mg, 4.0 mmol) in dry THF (5 mL) was stirred at room temperature. DMF (0.025 mL) was added through a silica gel filter, and the mixture was stirred at room temperature for 30 min. The reaction mixture was evaporated in vacuo to obtain the acid chloride. A solution of hexyl anthranilate (443 mg, 2.0 mmol) and triethylamine (405 mg, 4.0 mmol) in dry THF (10 mL) was added to the evaporated residue. The mixture was stirred at room temperature for 40 min. CH_2Cl_2 (30 mL) was added to the mixture, and then the solution was washed with 1 N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and H_2O (20 mL). The organic layer was evaporated and then purified by column chromatography (silica gel, 1/3 = AcOEt/CH_2Cl_2) to obtain the desired compound as a light brown powder (390 mg, 51%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.08 (s, 1H, benzamide), 8.87 (d, J = 8.1 Hz, 1H), 8.40 (s, 1H, acetamide), 8.06 (dd, J = 8.0, 1.3 Hz, 1H), 7.99 (d, J = 8.7 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.10 (t, J = 7.7 Hz, 1H), 4.33 (t, J = 6.6 Hz, 2H), 2.09 (s, 3H), 1.77 (q, J = 6.8 Hz, 2H), 1.44 (m, 2H), 1.34 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 168.7, 165.3, 141.82, 141.76, 134.6, 131.0, 130.0, 128.5, 122.6, 120.4, 119.4, 115.6, 65.8, 31.5, 28.5, 25.7, 24.7, 22.6, 14.1; IR (2 mM in CH_2Cl_2) 3427, 3306, 3266, 1675, 1608, 1590, 1512 cm^{-1}; HRMS *m*/*e* calcd for $C_{22}H_{26}N_2O_4$: 382.1893, found 382.1874.

2-Nitroterephthalic Acid 4-Methyl Ester (17). A solution of nitroterephthalic acid (21.1 g, 100 mmol) and concentrated H_2SO_4 (5 mL) in MeOH (100 mL) was refluxed for 75 min. The mixture was cooled to room temperature, and the solvent was evaporated in vacuo. The residue was dissolved in aqueous $NaHCO_3$ (300 mL) and washed with CH_2Cl_2 (200 mL). The aqueous layer was acidified with concentrated HCl to pH = 2 and then extracted with AcOEt (3 × 150 mL). The organic layers were combined, washed with brine (150 mL), and dried over $MgSO_4$. The organic layer was evaporated in vacuo and recrystallized from H_2O (500 mL) to give the titled product as white crystals (16.1 g, 71%): mp 134−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, J = 1.4 Hz, 1H), 8.37 (dd, J = 8.1, 1.3 Hz, 1H), 7.96 (d, 8.1, 1H), 4.02 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.2, 164.2, 148.7, 134.5, 133.6, 130.7, 129.5, 125.1, 53.3; HRMS *m*/*e* calcd for $C_9H_7NO_6$ 225.0273, found 225.0265.

2-Nitrobenzoic Acid 1-Hexyl Ester. To a solution of 2-nitrobenzoic acid (33.4 g, 200 mmol) in 1-hexanol (200 mL) was added toluene (140 mL) and concentrated H_2SO_4 (1 mL), and the mixture was refluxed for 2 h. The mixture was cooled to room temperature and washed with saturated aqueous $NaHCO_3$ (400 mL) and brine (400 mL). The organic layer was dried over $MgSO_4$, and the drying reagent was filtered off. The filtrate was evaporated in vacuo to give the titled product as an amber oil (42.3 g, 84%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 6.6 Hz, 3H), 1.36 (m, 6H), 1.72 (p, J = 7.0 Hz, 2H), 4.33 (t, J = 6.8 Hz, 2H), 7.63 (td, J = 7.4, 1.7 Hz, 1H), 7.68 (td, J = 7.6, 1.5 Hz, 1H), 7.76 (dd, J = 7.3, 1.8 Hz, 1H), 7.90 (dd, J = 7.6, 1.7 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 148.1, 132.6, 129.6, 127.3, 123.5, 70.6, 31.4, 31.1, 28.0, 25.2, 22.4, 22.2, 13.7; LRMS (FAB, MNBA) *m*/*e* calcd for $C_{13}H_{18}NO_4$ (M + H$^+$) 252.1, found 252.

2-Aminobenzoic Acid 1-Hexyl Ester. A solution of 1-hexyl nitrobenzoate (12.6 g, 50 mmol) and 10% Pd/C (500 mg) in MeOH (50 mL) was prepared in a 250-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously for 3 h at room temperature. The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give the desired compound as an orange oil (11.5 g, 100%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.6, 1.4 Hz, 1H), 7.26 (td, J = 7.7, 1.5 Hz, 1H), 6.64 (m, 2H), 4.26 (t, J = 6.6 Hz, 2H), 1.75 (q, J = 7.0 Hz, 2H), 1.40 (m, 6H), 0.90 (t, J = 6.2 Hz, 3H).

General Synthesis of Functionalized Linear Strand (21). The functionalized linear strand **21** from 1-hexyl anthranilate was synthesized by the sequential transformations analogous to linear strand **14** from methyl anthranilate, couplings with nitro compounds and hydrogenations.

General Coupling Method for 21. To a solution of nitro compound (2-nitrobenzoic acid or **17**, 10 mmol) and oxalyl chloride (2.40 g, 20 mmol) in dry THF (20 mL) was added DMF (0.1 mL) through a silica gel filter, and the mixture was stirred at room temperature for 30 min. The reaction mixture was evaporated in vacuo to obtain the acid chloride. To a solution of the amine (10 mmol) and pyridine (1.58 g, 20 mmol) in CH_2Cl_2 was added a solution of the acid chloride in dry CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature overnight. CH_2Cl_2 (200 mL) was added to the mixture which was then washed with 1 N HCl (2 × 200 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give the crude material.

General Hydrogenation Method for 21. A solution of nitro compound (6.0 mmol) and 10% Pd/C (300 mg) in dry CH_2Cl_2 (40 mL) was prepared in a 100-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously overnight at room temperature.

The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give the desired compound.

2-(2-Nitro-4-methoxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester (18). The crude product was purified by column chromatography (silica gel, CH_2Cl_2) to obtain the desired product as a yellow wax (89%): mp 99−100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.71 (s, 1H, amide), 8.79 (d, J = 6.9 Hz, 1H), 8.72 (s, 1H), 8.39 (d, J = 7.5 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 4.28 (t, J = 6.6 Hz, 2H), 4.01 (s, 3H), 1.73 (q, J = 7.0 Hz, 2H), 1.38 (m, 6H), 0.90 (t, J = 6.6 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.5, 164.2, 163.5, 147.0, 140.8, 136.3, 134.8, 134.5, 132.8, 130.9, 128.7, 125.8, 123.6, 120.7, 115.8, 65.8, 53.0, 31.4, 28.4, 25.6, 22.5, 14.0; HRMS *m*/*e* calcd for $C_{22}H_{24}N_2O_7$: 428.1584, found 428.1587.

2-(2-Amino-4-methoxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester (19). The filtrate was introduced in the next step directly.

2-(2-(2-Nitrobenzoylamino)-4-methoxycarbonylbenzoylamino)-benzoic Acid 1-Hexyl Ester (20). Recrystallized from AcOEt and hexane to obtain the desired product as yellow fine needles (78%): mp 148−149 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.33 (s, 1H, amide), 11.72 (s, 1H, amide), 9.40 (s, 1H), 8.66 (d, J = 8.4 Hz, 1H), 8.10 (td, J = 7.1, 1.7 Hz, 2H), 8.00 (m, 2H), 7.74 (m, 2H), 7.65 (m, 1H), 7.58 (td, J = 8.0, 1.5 Hz, 1H), 7.18 (td, J = 7.7, 0.6 Hz, 1H), 4.37 (t, J = 6.8 Hz, 2H), 4.00 (s, 3H, methoxy), 1.80 (q, J = 7.0 Hz, 2H), 1.38 (m, 6H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.6, 166.8, 165.9, 164.3, 147.0, 140.6, 140.0, 134.6, 134.2, 133.8, 132.8, 131.1, 131.0, 128.5, 127.3, 124.9, 124.7, 124.1, 123.7, 122.7, 120.6, 116.2, 66.1, 52.6, 31.4, 28.5, 25.7, 22.5, 14.0; HRMS *m*/*e* calcd for $C_{29}H_{29}N_3O_8$: 547.1955, found 547.1945.

2-(2-(2-Aminobenzoylamino)-4-methoxycarbonylbenzoylamino)-benzoic Acid 1-Hexyl Ester: A yellow powder (100%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.27 (s, 1H, amide), 11.85 (s, 1H, amide), 9.35 (d, J = 1.5 Hz, 1H), 8.83 (dd, J = 8.4, 0.6 Hz, 1H), 8.11 (dd, J = 8.0, 1.7 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.90 (dd, J = 8.3, 1.7 Hz, 1H), 7.74 (dd, J = 8.1, 1.5 Hz, 1H), 7.64 (td, J = 8.4, 1.5 Hz, 1H), 7.26 (td, J = 7.8, 1.5 Hz, 1H), 7.19 (td, J = 8.0, 0.9 Hz, 1H), 6.78 (td, J = 8.0, 0.9 Hz, 1H), 6.71 (d, J = 8.1 Hz, 1H), 4.36 (t, J = 6.6 Hz, 2H), 3.97 (s, 3H), 1.80 (q, J = 7.4, 1.40, m Hz, 6H), 0.91 (t, J = 7.8 Hz, 3H).

2-(2-(2-(2-Nitro-4-methoxycarbonylbenzoylamino)benzoylamino)-4-methoxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester. The crude product was purified by column chromatography (silica gel, 1/50 = MeOH/CH_2Cl_2) to obtain the desired product (62%): mp 206 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.37 (s, 1H, amide), 12.29 (s, 1H, amide), 11.95 (s, 1H, amide), 9.18 (d, J = 1.5 Hz, 1H), 8.82 (d, J = 8.4 Hz, 2H), 8.73 (d, J = 1.2 Hz, 1H), 8.39 (dd, J = 7.5, 1.4 Hz, 1H), 8.13 (dd, J = 7.8, 1.5 Hz, 1H), 7.96 (m, 3H), 7.81 (d, J = 7.8 Hz, 1H), 7.64 (m, 2H), 7.34 (t, J = 7.7 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 4.36 (t, J = 6.8 Hz, 2H), 4.10 (s, 3H), 3.95 (s, 3H), 1.8 (q, J = 7.1 Hz, 2H), 1.36 (m, 6H), 0.91 (t, J = 7.1 Hz, 3H); HRMS *m*/*e* calcd for $C_{38}H_{36}N_4O_{11}$ 724.2381, found 724.2366.

2-(2-(2-(2-Amino-4-methoxycarbonylbenzoylamino)benzoylamino)-4-methoxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester. The filtrate was introduced directly to the next step.

2-(2-(2-(2-(1-Hexanoyl)amino-4-methoxycarbonylbenzoylamino)-benzoylamino)-4-methoxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester (21). To a solution of the aforementioned amine (2.0 mmol) and pyridine (400 mg, 5.0 mmol) in CH_2Cl_2 was added a solution of hexanoyl chloride (538 mg, 4.0 mmol) in dry CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature for 1 h. CH_2Cl_2 (50 mL) was added to the mixture which was then washed with 1 N HCl (2 × 100 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$, evaporated in vacuo, and recrystallized from CH_2Cl_2 (60 mL) and hexane (440 mL) to obtain the desired product as yellow fine needles (1.31 g, 84%): mp 175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.38 (s, 2H, amide), 12.32 (s, 1H, amide), 11.11 (s, 1H, amide), 9.31 (s, 1H), 9.28 (s, 1H), 8.79 (d, J = 8.4 Hz, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.97 (m, 4H), 7.87 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 7.8 Hz, 2H), 7.33 (t, J = 7.7 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 4.35 (t, J = 6.6 Hz, 2H), 4.00 (s, 3H), 3.94 (s, 3H), 2.43 (t, J = 7.5 Hz, 2H), 1.77 (m, 4H), 1.36 (m, 10H), 0.90 (m, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 172.3, 168.7, 167.7, 167.1 (2), 166.3, 166.0, 140.7, 140.4, 139.9, 139.7, 134.8, 134.2, 133.9, 133.3, 131.2, 127.7, 127.6 (2), 125.1, 124.9, 124.4, 124.1, 124.0, 123.8, 123.2, 122.4, 122.0, 121.1, 120.8, 116.2, 66.2, 52.8, 52.5, 38.5, 31.4, 28.5, 25.7, 25.1, 22.6, 22.5, 14.0; IR (2 mM in CH_2Cl_2) 3259, 1726, 1689, 1659, 1604, 1578, 1519 cm^{-1}; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{44}H_{49}N_4O_{10}$ (M + H$^+$) 793.3449, found 793.3454

2-(2-(2-(2-(1-Hexanoyl)amino-4-hydroxycarbonylbenzoylamino)-benzoylamino)-4-hydroxycarbonylbenzoylamino)benzoic Acid 1-Hexyl Ester (22). To a solution of **21** (935 mg, 1.2 mmol) in THF (48 mL) was added 0.5 N aqueous LiOH (16 mL), and the reaction mixture was stirred at −8 °C for 54 h. Hexane (200 mL) and 1 N HCl (200 mL) were added. The precipitate was collected on a glass filter and washed with H_2O (40 mL) and then hexane (40 mL). The residue was purified by column chromatography (silica gel, 7/30/60 = NH_4OH/MeOH/CH_2Cl_2) to obtain the desired product (806 mg, 89%): mp 268−270 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.31 (s, 2H, acid), 11.43 (s, 1H, amide), 11.40 (s, 1H, amide), 11.30 (s, 1H, amide), 10.37 (s, 1H, amide), 8.72 (s, 1H), 8.66 (s, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.90 (m, 4H), 7.75 (d, J = 8.1 Hz, 1H), 7.59 (m, 3H), 7.33 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 4.14 (t, J = 6.5 Hz, 2H), 2.16 (t, J = 7.2 Hz, 2H), 1.58 (q, J = 7.2 Hz, 2H), 1.44 (q, J = 6.9 Hz, 2H), 1.93 (m, 10H), 0.78 (m, 6H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 171.3, 167.2, 166.9, 166.5, 166.4, 165.9 (2), 139.1, 137.8, 137.5, 137.0, 134.0 (2), 133.6, 132.3, 130.6, 128.6 (2), 128.4 (2), 127.3, 125.4, 125.0, 124.7, 124.1, 123.8 (2), 123.2, 122.4, 121.9, 118.7, 65.3, 36.7, 30.9, 30.7, 27.9, 25.1, 24.5, 21.9, 13.9; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{42}H_{44}N_4O_{10}Na$ (M + Na$^+$) 787.2955, found 787.2944.

2-Nitroterephthalic Acid 4-(2,6-Dimethy-4-heptyl) Ester. 2-Nitroterephthalic Acid Bis-(2,6-dimethyl-4-heptyl) Ester. To a solution of nitroterephthalic acid (21.1 g, 100 mmol) in 2,6-dimethyl-4-heptanol (200 mL) was added toluene (200 mL) and sulfuric acid (3 g), and the mixture was refluxed for 7.5 h. The mixture was cooled to room temperature, and AcOEt (600 mL) was added. The organic phase was washed with H_2O (1000 mL) and brine (500 mL) and dried over $MgSO_4$. The solvent was evaporated in vacuo to give the crude mixture of the titled compounds. The crude product was separated by column chromatography (silica gel, CH_2Cl_2 and then 1/6 = MeOH/CH_2Cl_2) to give the monoester as a brown oil (19.7 g, 58%) and the diester as a yellow oil (19.3 g, 42%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 1.1 Hz, 1H), 8.35 (dd, J = 8.1, 1.2 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.80 (broad s, 1H, acid), 5.38 (m, 1H), 1.69 (m, 4H), 1.43 (m, 2H), 0.95 (m, 12H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 163.5, 148.6, 134.9, 133.6, 130.6, 129.7, 124.9, 74.1, 43.9, 24.8, 23.2, 22.3.

2-Aminoterephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester. A solution of 2-nitroterephthalic acid bis-(2,6-dimethy-4-heptyl) ester (17.4 g, 40 mmol) and 10% Pd/C (700 mg) in dry THF (80 mL) was prepared in a 250-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously overnight at room temperature. The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give the desired compound as a yellow oil (16.7 g, 95% NMR purity, 91%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 1H), 7.34 (s, 1H), 7.25 (dd, J = 7.5, 1.4 Hz, 1H), 5.78 (broad s, 2H, amine), 5.30 (m, 2H), 1.66 (m, 8H), 1.40 (m, 4H), 0.94 (m, 24H).

General Synthesis of Functionalized Linear Strand (23). The functionalized linear strand **23** from 2-aminoterephthalic acid bis-(2,6-dimethy-4-heptyl) ester was synthesized by the sequential transformations analogous to functionalized linear strand **21**. In the synthesis of **23**, 2-nitroterephthalic acid 4-(2,6-dimethy-4-heptyl) ester was used for couplings instead of 2-nitrobenzoic acid.

General Coupling Method for 23. To a solution of 2-nitroterephthalic acid 4-(2,6-dimethy-4-heptyl) ester or **17** (10 mmol) and oxalyl chloride (2.40 g, 20 mmol) in dry THF (20 mL) was added DMF (0.1 mL) through a silica gel filter, and the mixture was stirred at room temperature for 30 min. The reaction mixture was evaporated in vacuo to obtain the acid chloride. To a solution of the amine (10 mmol) and pyridine (1.58 g, 20 mmol) in CH_2Cl_2 was added a solution of the acid chloride in dry CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature overnight. CH_2Cl_2 (200 mL) was added to the mixture which was then washed with 1 N HCl (2 × 200 mL), saturated aqueous

$NaHCO_3$ (200 mL), and brine (200 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give the crude material.

General Hydrogenation Method for 23. A solution of nitro compound (20 mmol) and 10% Pd/C (450 mg) in dry THF (50 mL) was prepared in a 100-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously overnight at room temperature. The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give the desired compound.

2-(2-Nitro-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester. The crude product was purified by column chromatography (silica gel, CH_2Cl_2) to obtain the desired product as a yellow oil (89%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.67 (s, 1H, amide), 9.37 (s, 1H), 8.75 (d, J = 1.2 Hz, 1H), 8.41 (dd, J = 7.8, 1.5 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.83 (m, 2H), 5.32 (m, 2H), 4.02 (s, 3H), 1.66 (m, 8H), 1.41 (m, 4H), 0.93 (m, 24H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.4, 165.1, 164.2, 163.6, 146.9, 140.9, 136.3, 134.6, 132.9, 130.8, 128.9, 125.9, 124.3, 121.8, 119.2, 73.7, 73.0, 53.0, 43.9, 24.8, 23.1, 22.4; HRMS *m*/*e* calcd for $C_{35}H_{48}N_2O_9$ 640.3360, found 640.3347.

2-(2-Amino-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester: a yellow oil (99%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.99 (s, 1H, amide), 9.43 (d, J = 1.5 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.77 (m, 2H), 7.43 (m, 2H), 6.08 (broad s, 2H, amine), 5.35 (m, 2H), 3.93 (s, 3H), 1.69 (m, 8H), 1.44 (m, 4H), 0.95 (m, 24H).

2-(2-(2-Nitro-4-(2,6-dimethy-4-heptyl)benzoylamino)-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester. The crude product was purified by column chromatography (silica gel, 1/3 = diethyl ether/hexane) to give the desired product as a yellow foam (54%): mp 63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.41 (s, 1H, amide), 11.91 (s, 1H, amide), 9.43 (s, 1H), 9.32 (s, 1H), 8.73 (s, 1H), 8.42 (d, J = 7.8 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.01 (s, 2H), 7.81 (m, 2H), 5.41 (m, 2H), 5.29 (m, 1H), 3.99 (s, 3H), 1.70 (m, 12H), 1.42 (m, 6H), 0.96 (m, 36H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.7, 166.8, 165.9, 165.1, 163.8, 163.5, 147.0, 140.8, 140.1, 136.1, 136.0, 134.7, 134.5, 133.6, 131.0, 128.8, 127.4, 125.8, 125.2, 124.1, 123.7, 122.8, 121.8, 119.5, 74.0, 73.6, 73.1, 52.6, 43.8, 24.8, 23.1, 22.3; LRMS (FAB, MNBA) *m*/*e* calcd for $C_{52}H_{71}N_3O_{12}Na$ (M + Na^+) 952.5, found 952.7.

2-(2-(2-Amino-4-(2,6-dimethy-4-heptyl)benzoylamino)-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester: a yellow foam (100%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.33 (s, 1H, amide), 12.04 (s, 1H, amide), 9.42 (s, 1H), 9.36 (s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.97 (m, 2H), 7.82 (d, J = 9.0 Hz, 2H), 7.46 (m, 2H), 5.35 (m, 3H), 3.99 (s, 3H), 1.70 (m, 12H), 1.40 (m, 6H), 0.95 (m, 36H).

2-(2-(2-(2-Nitro-4-methoxycarbonylbenzoylamino)-4-(2,6-dimethy-4-heptyl)benzoylamino)-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester. The crude product was crystallized from trace CH_2Cl_2, diethyl ether, and hexane in a freezer to obtain the desired product (60%): mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.44 (s, 1H, amide), 12.42 (s, 1H, amide), 11.80 (s, 1H, amide), 9.42 (d, J = 1.2 Hz, 1H), 9.40 (s, 1H), 9.20 (s, 1H), 8.75 (d, J = 1.5 Hz, 1H), 8.40 (dd, J = 8.0, 1.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.00 (m, 4H), 7.83 (m, 2H), 5.39 (m, 3H), 4.02 (s, 3H), 3.96 (s, 3H), 1.66 (m, 12H), 1.44 (m, 6H), 0.96 (m, 36H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.7, 167.0, 166.9, 165.8, 165.1, 165.0, 164.3, 163.6, 146.8, 140.7, 140.0, 139.6, 136.4, 136.2, 135.3, 134.7, 134.2, 132.8, 131.1, 129.0, 127.6, 127.5, 125.9, 125.2, 124.7, 124.4, 123.6, 123.1, 121.8, 119.5, 74.0, 73.2, 72.8, 53.0, 43.9, 24.8, 23.2, 22.4; LRMS (FAB, MNBA) *m*/*e* calcd for $C_{61}H_{78}N_4O_{15}Na$ (M + Na^+) 1129.5, found 1130.

2-(2-(2-(2-Amino-4-methoxycarbonylbenzoylamino)-4-(2,6-dimethy-4-heptyl)benzoylamino)-4-methoxycarbonylbenzoylamino)-terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester: a yellow foam (100%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.42 (s, 1H, amide), 12.36 (s, 1H, amide), 12.03 (s, 1H, amide), 9.41 (s, 1H), 9.37 (s, 1H), 9.32 (s, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.01 (m, 4H), 7.84 (d, J = 9.0 Hz, 2H), 7.51 (s, 1H), 5.37 (m, 3H), 4.02 (s, 3H), 3.93 (s, 3H), 1.72 (m, 12H), 1.44 (m, 6H), 0.96 (m, 36H).

2-(2-(2-(2-(1-Hexanoyl)amino-4-methoxycarbonylbenzoylamino)-4-(2,6-dimethy-4-heptyl)benzoylamino)-4-methoxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester (23). To a solution of tetraanthranilamide (5.22 g, 4.8 mmol) and pyridine (949 mg, 12 mmol) in CH_2Cl_2 (20 mL) was added a solution of 1-hexanoyl chloride (1.35 g, 10 mmol) in dry CH_2Cl_2 (20 mL), and the mixture was stirred at room temperature for 3 h. CH_2Cl_2 (250 mL) was added to the mixture which was then washed with 1 N HCl (200 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give the crude product (6.22 g). The crude product was purified by column chromatography (silica gel, 1/5 = diisopropyl ether/toluene) to give the desired product as a yellow foam (3.86 g, 69%): mp 159−161 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.44 (s, 2H, amide), 12.26 (s, 1H, amide), 11.15 (s, 1H, amide), 9.41 (d, J = 1.2 Hz, 1H), 9.37 (d, J = 1.2 Hz, 1H), 9.33 (d, J = 1.5 Hz, 1H), 9.31 (s, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.00 (m, 5H), 7.84 (m, 2H), 5.37 (m, 3H), 4.01 (s, 3H), 3.94 (s, 3H), 2.45 (t, J = 7.7 Hz, 2H), 1.73 (m, 14H), 1.42 (m, 10H), 0.97 (m, 39H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 172.4, 167.7, 167.1, 167.0, 166.3, 165.9, 165.1, 140.7, 140.6, 139.9, 139.7, 136.2, 135.1, 134.4, 134.1, 131.1, 127.7, 127.5, 125.4, 124.9, 124.7, 124.3, 124.0, 123.6, 123.3, 122.5, 121.8, 119.5, 74.1, 72.9, 52.8, 43.8, 38.5, 31.4, 24.9, 23.2, 22.5; IR (2 mM in CH_2Cl_2) 3258, 1722, 1689, 1659, 1576, 1522 cm^{-1}; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{67}H_{90}N_4O_{14}Na$ (M + Na^+) 1197.6351, found 1197.6397.

2-(2-(2-(2-(1-Hexanoyl)amino-4-hydroxycarbonylbenzoylamino)-4-(2,6-dimethy-4-heptyl)-benzoylamino)-4-hydroxycarbonylbenzoylamino)terephthalic Acid Bis-(2,6-dimethy-4-heptyl) Ester (24). To a solution of the dimethyl ester **23** (1.90 g, 1.61 mmol) in THF (100 mL) was added 0.5 N aqueous LiOH (50 mL), and the reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo. CH_2Cl_2 (500 mL) added to the residue which was then washed with 1 N HCl (300 mL) and brine (300 mL). The organic layer was dried over sodium sulfate and evaporated in vacuo to give the crude product (1.80 g). The crude product was purified by column chromatography (silica gel, 1/10/20 = NH_4OH/MeOH/CH_2Cl_2) to give the desired product as a yellow foam (813 mg, 44%): mp 246−248 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.94 (s, 1H, amide), 12.84 (s, 1H, amide), 12.58 (s, 1H, amide), 11.45 (s, 1H, amide), 9.78 (s, 1H), 9.58 (s, 1H), 9.55 (s, 1H), 9.48 (s, 1H), 8.21 (dd, J = 8.4, 1.8 Hz, 2H), 8.13 (m, 4H), 8.00 (d, J = 8.1 Hz, 1H), 7.88 (dd, J = 5.4, 1.2 Hz, 1H), 5.41 (m, 3H), 2.52 (t, J = 7.5 Hz, 2H), 1.76 (m, 12H), 1.43 (m, 12H), 0.99 (m, 39H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 172.5, 172.0, 171.7, 167.8, 167.2, 166.9, 165.2, 141.0, 140.8, 140.2, 136.2, 135.2, 133.9, 133.2, 131.2, 128.9, 127.7, 127.6, 125.8, 124.7, 124.5, 124.0, 123.4, 123.1, 122.8, 121.9, 119.6, 74.2, 73.3, 73.0, 44.0, 38.6, 31.5, 29.8, 24.9, 23.3, 22.6, 14.1; IR (2 mM in CH_2Cl_2) 3199, 1704, 1657, 1575, 1525 cm^{-1}; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{65}H_{86}N_4O_{14}Na$ (M + Na^+) 1169.6038, found 1169.6029.

2,6-Bis-(2-(2-methoxycarbonylphenylcarbamoyl)phenylcarbamoyl)pyridine (31). To a solution of 2,6-pyridinecarboxylic acid (167 mg, 1.0 mmol) and oxalyl chloride (380 mg, 3.0 mmol) in dry THF (5 mL) was added DMF (0.025 mL) through a silica gel filter, and the reaction mixture was stirred at room temperature for 20 min. The mixture was evaporated in vacuo to obtain the acid chloride. To a solution of **8** (541 mg, 2.0 mmol) and pyridine (237 mg, 3.0 mmol) in dry THF (5 mL) was added the acid chloride in dry THF (5 mL), and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture was added to chloroform (40 mL) and washed with 1 N HCl (2 × 20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), and H_2O (2 × 20 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give the crude product. The crude product was recrystallized from $CHCl_3$ (30 mL) and hexane (80 mL) to obtain the desired compound as brown needles (508 mg, 76%): mp 241−242 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.08 (s, 2H, pyridinedicarboxamide), 11.60 (s, 2H, anthranilamide), 8.88 (d, J = 8.1 Hz, 2H), 8.48 (m, 4H), 8.13 (t, J = 7.8 Hz, 1H), 7.90 (dd, J = 8.1, 1.5 Hz, 2H), 7.62 (m, 4H), 7.22 (t, J = 7.7 Hz, 2H), 6.75 (t, J = 6.2 Hz, 2H), 6.70 (t, J = 8.0 Hz, 3H), 3.78 (s, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.3, 166.5, 162.1, 149.5, 141.1, 139.2 (2), 134.3, 132.6, 130.5, 127.5, 124.9, 123.6, 122.6, 122.2, 121.8, 120.0, 114.3, 52.2; IR (2 mM in CH_2Cl_2) 3270, 1693, 1608, 1585, 1532 cm^{-1}; HRMS *m*/*e* calcd for $C_{37}H_{29}N_5O_8$

671.2016, found 671.2107. Anal. calcd for $C_{37}H_{29}N_5O_8$: C, 66.16; H, 4.35; N, 10.43. Found: C, 65.87; H, 4.36; N, 10.29.

2,6-Pyridinedicarboxylic Acid *N*-Oxide (26). 2,6-Pyridinedicarboxylic acid (8.81 g) was dissolved in H_2O_2 (50 mL) and AcOH (20 mL), and the mixture was stirred at 100 °C for 6 h. The reaction mixture was evaporated and solidified from THF (100 mL) and hexane (150 mL). The solid was collected and washed with hexane (2 × 30 mL) to obtain the desired compound as a white solid (5.46 g, 60%): mp 155−157 °C (lit.[21c] 155−157 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.23 (d, J = 7.8 Hz, 2H), 7.94 (t, J = 8.0 Hz, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 161.0, 139.4, 132.4, 129.0; HRMS *m*/*e* calcd for $C_7H_5NO_5$ 183.0168, found 183.0171. Anal. calcd for $C_7H_5NO_5$: C, 45.91; H, 2.75; N, 7.65. Found: C, 46.00; H, 2.73; N, 7.70.

2,6-Bis-(2-(2-methoxycarbonylphenylcarbamoyl)phenylcarbamoyl)pyridine *N*-Oxide (32). To a solution of **26** (101 mg, 0.55 mmol) and oxalyl chloride (190 mg, 1.5 mmol) in dry THF (3 mL) was added DMF (0.025 mL) through a silica gel filter, and the reaction mixture was stirred at room temperature for 10 min. The mixture was evaporated in vacuo to obtain the acid chloride as a yellow oil. To a solution of **8** (270 mg, 1 mmol) and pyridine (119 mg, 1.5 mmol) in dry THF (3 mL) was added the acid chloride in dry THF (5 mL) dropwise, and the resulting mixture was stirred at room temperature overnight. 1 N HCl (50 mL) was added to the mixture which was then extracted with AcOEt (50 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL). The precipitation was collected on a glass filter, and the organic layer was washed with brine. The filtered residue and the organic layer were combined and evaporated. The evaporated residue was dissolved in $CHCl_3$, washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give the crude product. The crude product was recrystallized from $CHCl_3$ (15 mL) and hexane (50 mL). The second recrystallization was performed from $CHCl_3$ (20 mL) and hexane (50 mL) to obtain the desired compound as white crystals (238 mg, 69%): mp 247−249 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.80 (s, 2H, pyridinedicarboxamide), 11.78 (s, 2H, anthranilamide), 8.88 (d, J = 8.4 Hz, 2H), 8.60 (m, 4H), 7.88 (m, 4H), 7.58 (m, 2H), 7.32 (m, 4H), 4.92. t (7.5, 2H), 3.89 (s, 6H, methyl); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.9, 166.2, 158.0, 142.4, 141.5, 137.4, 134.7, 132.1, 131.4, 130.6, 127.5, 127.0, 126.1, 125.0, 124.1, 122.5, 121.0, 115.1, 52.5; IR (2 mM in CH_2Cl_2) 3295, 3270, 1676, 1606, 1584, 1527 cm^{-1}; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{37}H_{30}N_5O_9$ (M + H^+) 688.2044, found 688.2037.

2,6-Bis-(4-(2-methoxycarbonylphenylcarbamoyl)phenylcarbamoyl)pyridine (34). To a solution of 2,6-pyridinedicarboxylic acid (167 mg, 1.0 mmol) and oxalyl chloride (381 mg, 3.0 mmol) in dry THF (5 mL) was added DMF (0.025 mL) through a silica gel filter, and the reaction mixture was stirred at room temperature for 30 min. The mixture was evaporated in vacuo to obtain the acid chloride. To a solution of methyl 4-aminobenzoylanthranilate (541 mg, 2.0 mmol) and pyridine (237 mg, 3.0 mmol) in dry THF (10 mL) was added the acid chloride in dry THF (5 mL) dropwise, and the resulting mixture was stirred at room temperature for 1 h. Hexane (40 mL) was added to the reaction mixture, and the precipitation was collected on a glass filter. The solid was washed with 1 N HCl (2 × 20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), and H_2O (2 × 20 mL). The crude product was solidified from DMSO (100 mL), MeOH (100 mL), and H_2O (50 mL) to obtain the desired compound as a pale yellow green powder (600 mg, 89%): mp 326−327 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.62 (s, 2H, amide), 11.31 (s, 2H, amide), 8.60 (d, J = 8.4 Hz, 2H), 8.47 (d, J = 7.5 Hz, 2H), 8.36 (t, J = 8.1 Hz, 1H), 8.21 (d, J = 8.4 Hz, 4H), 8.05 (m, 6H), 7.70 (t, J = 8.1 Hz, 2H), 7.25 (t, J = 7.5 Hz, 2H), 3.93 (s, 3H); LRMS (FAB, MNBA) *m*/*e* calcd for $C_{37}H_{30}N_5O_8$ (M + H^+) 672.2094, found 672.2066.

2,6-Bis-(4-(2-methoxycarbonylphenyl)carbamoyl)phenylcarbamoyl)pyridine *N*-Oxide (35). To a solution of 2,6-pyridinedicarboxylic acid *N*-oxide (181 mg, 1.0 mmol) and oxalyl chloride (381 mg, 3.0 mmol) in dry THF (5 mL) was added DMF (0.025 mL) through a silica gel filter, and the reaction mixture was stirred at room temperature for 30 min. The mixture was evaporated in vacuo to obtain the acid chloride as a yellow solid. To a solution of methyl 4-aminobenzoylanthranilate (541 mg, 2.0 mmol) and pyridine (237 mg, 3.0 mmol) in dry THF (5 mL) was added a solution of the acid chloride in dry THF (5 mL) dropwise, and the resulting mixture was stirred at room temperature for 1.5 h. Hexane (30 mL) was added to the reaction mixture, and the precipitate was collected on a glass filter. The solid was washed with 1 N HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and H_2O (2 × 30 mL). The crude product was recrystallized from DMSO (60 mL) and MeOH (20 mL) to obtain the desired compound as a white solid (518 mg, 75%): mp 299−300 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.51 (s, 2H, pyidinedicarboxamide), 11.58 (s, 2H, benzamide), 8.56 (d, J = 8.7 Hz, 2H), 8.33 (d, J = 7.8 Hz, 2H), 8.03 (m, 6H), 7.87 (t, 1H), 7.69 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 7.7 Hz, 2H); HRMS (FAB, MNBA) *m*/*e* calcd for $C_{37}H_{30}N_5O_9$ (M + H^+) 688.2044, found 688.2036.

2-Nitrobenzoylanilide. A solution of 2-nitrobenzoic acid (16.7 g, 100 mmol) and oxalyl chloride (14.0 g, 110 mmol) in dry CH_2Cl_2 (30 mL) was stirred and cooled in an ice bath. DMF (0.31 g, 4.0 mmol) was added dropwise through a silica gel filter, and then the reaction mixture was stirred at room temperature for 2 h. The mixture was evaporated in vacuo to obtain the acid chloride as a yellow oil (18.9 g, 102%). A solution of aniline (27.9 g, 300 mmol) in dry CH_2Cl_2 (50 mL) was stirred and cooled in a water bath. A solution of the acid chloride in dry CH_2Cl_2 (50 mL) was added dropwise, and the mixture was stirred at room temperature for 2 h. CH_2Cl_2 (350 mL) was added to the mixture which was then washed with 1 N HCl (150 mL), saturated aqueous $NaHCO_3$ (150 mL), and brine (150 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo to give crude product (11.6 g). The crude product was recrystallized from AcOEt (170 mL) and hexane (340 mL) to obtain the desired compound as pale yellow plates (9.39 g, 39%). Through the aqueous washing, a substantial amount of undissolved material was separated and collected with a glass filter. This solid showed the same TLC behavior as the organic layer, and recrystallization from AcOEt (170 mL) and hexane (340 mL) gave the desired compound as pale yellow needles (12.3 g, 51%; the total yield, 21.7 g, 90%): mp 156−157 °C (lit.[30] 152−153 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.67 (s, 1H, amide), 8.14 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 6.3 Hz, 1H), 7.77 (m, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.36 (t, J = 8.0 Hz, 2H), 7.11 (t, J = 7.8 Hz, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 164.1, 146.5, 138.9, 134.1, 132.7, 131.0, 129.3, 128.8, 124.3, 124.0, 119.7; HRMS *m*/*e* calcd for $C_{13}H_{10}N_2O_3$ 242.0691, found 242.0692. Anal. calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.55; H, 4.20; N, 11.60.

2-Aminobenzoylanilide. A solution of 2-nitrobenzoylanilide (4.85 g, 20 mmol) and 10% Pd/C (0.97 g) in dry THF (30 mL) was prepared in a 100-mL round-bottomed flask provided with a magnetic stirrer. H_2 was introduced after removal of air by an aspirator, and the solution was stirred vigorously for 8 h at room temperature. The catalyst was removed by filtration through Celite. The filtrate was evaporated in vacuo to give the desired compound as a pale yellow wax (4.21 g, 99%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H, amide), 7.56 (d, J = 7.8 Hz, 1H), 7.48 (d, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.26 (t, J = 7.8 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 6.70 (m, 2H), 5.50 (s broad, 2H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 167.9, 149.8, 139.3, 132.1, 128.8, 128.6, 123.4, 120.5, 116.4, 115.3, 114.7.

2,6-Bis-(2-phenylcarbamoylphenylcarbamoyl)pyridine (36). To a solution of 2,6-pyridinedicarboxylic acid (0.84 g, 5.0 mmol) and oxalyl chloride (1.90 g, 15 mmol) in dry CH_2Cl_2 (20 mL) was added DMF (0.25 mL) dropwise through a silica gel filter, and the reaction mixture was stirred at room temperature for 4 h. The mixture was evaporated in vacuo to obtain the acid chloride as a yellow oil. To a solution of anthranylanilide (2.13 g, 10 mmol) and pyridine (1.19 g, 15 mmol) in dry CH_2Cl_2 (20 mL) was added the acid chloride (1.02 g, 5.0 mmol) in dry CH_2Cl_2 (20 mL) dropwise and the mixture was stirred at room temperature overnight. Saturated aqueous $NaHCO_3$ (50 mL) was added to the mixture, and the precipitation was collected. The residue was washed with H_2O (2 × 20 mL) and CH_2Cl_2 (2 × 20 mL). The crude product was dissolved in trace DMSO and recrystallized from THF (300 mL) and hexane (400 mL) to obtain the desired compound as white thin needles (2.55 g, 92%): mp 300−302 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.36 (s, 2H, amide), 10.33 (s, 2H, anilide), 8.34 (m, 5H), 7.83 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.8 Hz, 2H), 7.45 (m, 4H), 7.34 (t, J = 7.5 Hz, 2H), 6.87 (s, 6H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 166.2, 161.1, 148.4, 140.7, 138.5, 137.2, 131.8, 129.1, 124.9, 123.9, 121.9, 120.5; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{33}H_{26}N_5O_4$ (M + H^+) 556.1985, found 555.2010.

2,6-Bis-(2-phenylcarbamoylphenylcarbamoyl)pyridine *N*-Oxide (37). To a solution of **26** (0.55 g, 3.0 mmol) and oxalyl chloride (1.14 g, 9.0 mmol) in dry CH_2Cl_2 (10 mL) was added DMF (0.025 mL) through a silica gel filter, and the reaction mixture was stirred at room temperature for 5 min. The mixture was evaporated in vacuo to obtain the acid chloride (0.81 g) as a yellow oil. To a solution of anthranylaniline (1.27 g, 6.0 mmol) and pyridine (1.42 g, 18 mmol) in dry CH_2Cl_2 (20 mL) was added the acid chloride (0.81 g) in dry CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature overnight. 1 N HCl (30 mL) was added to the mixture, and the precipitate was collected on a glass filter. The residue was washed with saturated aqueous $NaHCO_3$ (2 × 15 mL), H_2O (2 × 15 mL), and CH_2Cl_2 (2 × 15 mL). The crude product was recrystallized from DMSO (8 mL), THF (80 mL), and hexane (80 mL) to obtain the desired compound as white crystals (0.90 g, 53%; first crop). The filtrate was evaporated and recrystallized from DMSO and H_2O as pale yellow thin needles (0.60 g, 35%; second crop): mp 243−245°; ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.75 (s, 2H, amide), 10.49 (s, 2H, anilide), 8.3 (d, J = 7.8 Hz, 2H), 8.20 (d, 8.1H), 7.70 (m, 7H), 7.61 (t, J = 7.8 Hz, 2H), 7.36 (t, 7.5Hz, 2H), 7.21 (t, J = 7.6 Hz, 4H), 7.01 (t, J = 7.4 Hz, 2H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 165.9, 157.9, 141.9, 138.9, 135.5, 131.1, 130.1, 128.6, 128.5, 128.2, 127.8, 124.8, 123.8, 123.5, 120.5; HRMS (FAB, MNBA) *m*/*e* calcd for $C_{33}H_{26}N_5O_5$ ($M + H^+$) 572.1934, found 572.1913.

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Supporting Information Available: Crystallographic details for oligoanthranilamides **15**, **31**, **32**, **36**, and **37** (Figures 1−5) including tables of atomic coordinates, thermal parameters, bond angles, and bond lengths (40 pages). Ordering information is given on any current masthead page.

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