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A highly stable double helix of aromatic oligoamide comprised of fused ring aromatic units

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ABSTRACT

Aromatic oligoamides of 2,6-diaminofluorobenzene and 1,8-diazafluoroanthrancene-2,7-diacid have been synthesized by a convergent method. The heptameric oligoamide can not only fold into a single helix but also hybridize into a highly stable double helix through intensive intermolecular aromatic stackings, which has been extensively characterized in the solid state by single crystal X-ray diffractions and in solution by ^{1}H NMR, NOESY, and UV/vis spectra. The K_{dim} values of the heptamer are over 10^7 L mol^{-1} in various solutions at rt. The extensive interstrand interactions, enlarged diameter (5.4 Å), and lower torsion angles (13°) render heptamer **1** readily to hybridize into a highly stable double helix based on spring-like extension mechanism.

1. Introduction

Helical structures as observed in biomacromolecules, such as proteins and DNA are ubiquitous, but play vital roles in their exquisite biological functions. For example, double helical structure of DNA is a key to genetic information storage, replication, and transcription. Inspired by such sophisticated structures and remarkable efficient hybridization of biomacromolecules, chemists have been engaged in developing a large number of artificial molecules with well-defined folded structures driven by noncovalent forces over the last decade.[1] Synthetic oligomers able to intertwine into multiple helices are of great interest because they might provide artificial molecular platforms to mimic folded structures and biological functions, for instance, double helical structure, information storage, and duplication in DNA, and also might have potential application in material sciences. Different types of multiple helical structures have been constructed so far by metal coordination, hydrogen bond, aromatic π–π stacking or salt bridge.[1,2] Metal coordination has proved effective for building helicates that were comprised of metal cations and organic ligands.[3] As for metal-free helix,[4] aromatic oligoamides represent one of most intensively studied foldamers, helical structures of which were usually driven by hydrogen bond and aromatic π–π stacking. Although many aromatic oligoamides have been found to display well-defined helical structures, only limited systems show tendency to aggregate into double, triple, and quadruple helices.[5,6] Other examples include oligoresorcinols,[7] ethynylhelicene oligomers,[8] *m*-terphenyl backbone oligomers exploiting amidinium–carboxylate salt bridges,[9] alternate sequences of aromatic hydrogen bond donors and acceptors.[10] However, much attention has been focused on the characterization of helical structures. Detailed understanding of the ability of foldamers to hybridize into double helices, a fundamental issue to the research of double helices, is still scarce. In this regard, oligoamides of 2,6-diaminopyridine and 2,6-pyridinedicarboxylic acid described by Huc and co-workers represent a significant advance.[5]

Several strategies including extending strand lengths, enlarging helical diameters or changing substituents[5,7] have been used to increase the stability of double helices. For instance, Huc demonstrated that oligoamides of 2,6-diaminopyridine and 2,6-pyridinedicarboxylic acid not only adopt a stable single helical conformation in solution as seen in other aromatic oligoamides foldamers, but also hybridize into double helical duplex. The dimerization constants of double helices increase on increasing the length of strands while the solution was equilibrated well.[5] The mechanism proposed for this hybridization involved a screw-like slippage in which the intrastrand interaction in single helix was destroyed in company with the simultaneous formation of

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interstrand interaction in double helices.[11] As a result of hybridization, a global and maximized intermolecular interaction in particular aromatic π–π stacking was achieved in double helices in comparison with in single helix. Although the hybridization was governed by many intrinsic factors, such as length of sequence and substituent of strand as well as extrinsic factors like solvent polarity and temperature, the formation of double helices is a highly cooperative process that is strictly controlled by the enthalpic gain and entropic loss during the hybridization.

We recently found that tetrameric and octameric amides of 7-amino-8-fluoro-2-quinolinecarboxylic acid with a large helical diameter exhibited a remarkable aggregation behavior.[6] That is, tetramer is able to adopt a helical conformation with a large pitch that allows the formation of an unprecedented quadruple helix and octamer dimerizes as a stable anti-parallel double helix. With the aim of investigating the formation of multiple helices of aromatic oligoamides, we became interested in the aromatic oligoamides sequences with more fused ring aromatic monomers. We anticipated that the large surface and size of the fused ring aromatic monomers render aromatic oligoamides to readily form stable double helices in view of the spring-like hybridization mechanism. Herein, we reported the design, synthesis, and hybridized behavior of a new series of oligoamide strands alternately consisting of 2,6-diaminofluorobenzene and 1,8-diazafluoroanthrancene-2,7-dicarboxylic acid; we notably showed that heptameric amide hybridized into a highly stable double helix in the solid phase and in solution via extensive intermolecular π-π stacking with dimerization constant K_{dim} over 10^7 L mol^{-1} in various solvents at rt.

2. Results and discussion

2.1. Design and synthesis

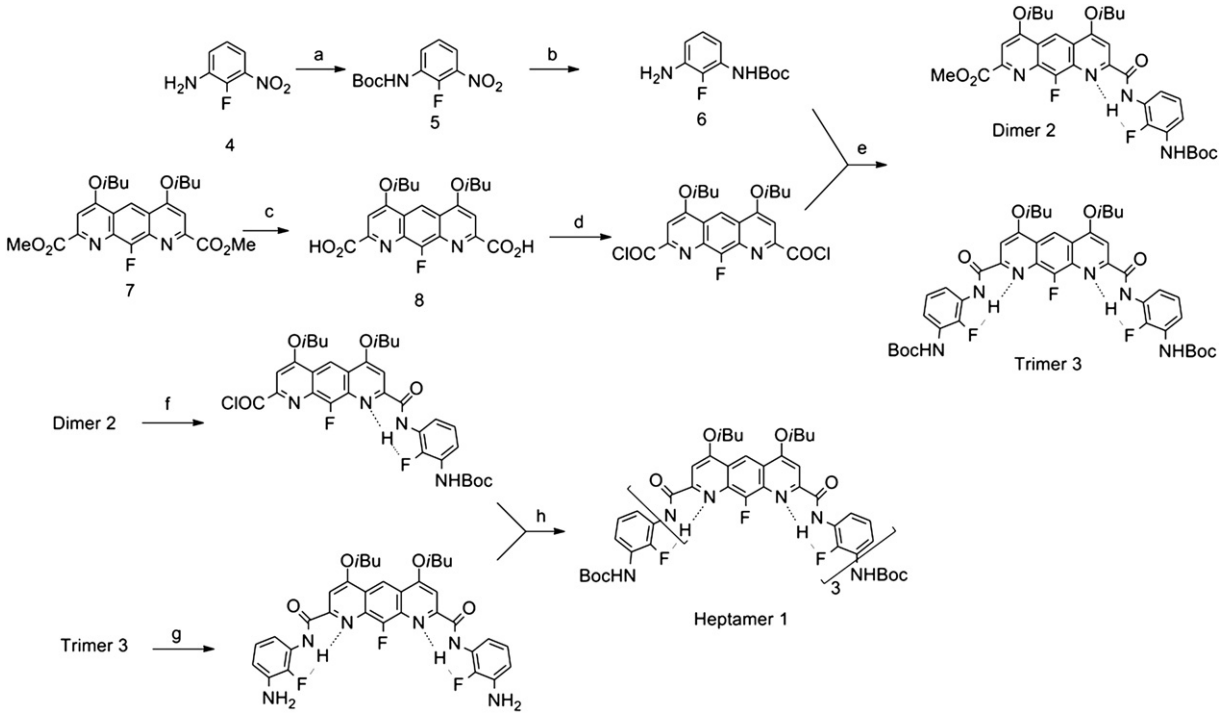
The structures of the aromatic oligoamides and their synthetic procedures were listed in Scheme 1. We chose a three fused aromatic ring for the present study because the fused ring aromatic monomer not only provides a large surface that is favorable for aromatic π–π stacking during the formation of double helices, but also possesses a large helical diameter in comparison with a single aromatic ring so as to lower the enthalpic cost of spring-like extension.[5,6] Moreover, foldamers containing a few units of fused aromatic ring have been less studied.[5,12] Initially, we have designed a series of the oligoamides comprised of only fused ring aromatic units, i.e., the oligoamides of 1,8-diazafluoro-anthrancene-2,7-dicarboxylic acid and 1,8-diazafluoroanthrancene-2,7-diamine. It turned out that the syntheses of such arylamides were very efficient for short strands like trimer but became very difficult for long strands like pentamer and heptamer, presumably due to the strong aromatic stacking in methylene chloride solution that hinders the effective elongation of the strand. To overcome this synthetic hindrance, we used 2,6-diaminofluorobenzene instead of 1,8-diazafluoro-anthrancene-2,7-diamine to reduce aromatic interaction and designed new oligoamide strands alternately consisting of 2,6-diaminofluorobenzene and 1,8-diazafluoroanthrancene-2,7-dicarboxylic acid. Moreover, the fluorine atom in fluorobenzene provides a hydrogen bond acceptor so that the protons of amides can readily form a three center hydrogen bond that also contributes to the stability of helix. As expected, the synthesis of heptamer **1** via a convergent approach as shown in Scheme 1 was smooth. Although diester **7** was easily prepared according to the procedure reported by us,[13] mono-saponification of diester **7** was found to produce monoacid in a very low yield due to the poor solubility in most common organic solvents (MeOH, THF, DMF). This situation renders it infeasible to prepare dimer **2** through the coupling of monoacid and monoamine **6**. Fortunately, we found that diester **7** could be easily hydrolyzed to generate 1,8-diazafluoroanthrancene-2,7-dicarboxylic acid **8** with quantitative yield. Afterward, the activation of diacid **8** was carried out in the presence of Ghosez reagent to generate diacid chloride that was directly coupled with monoamine **6** to generate trimer **3**. However, if a small amount of methanol was added into the reaction solution to quench the acid chloride after the coupling reaction proceeded for a certain time, dimer **2** and trimer **3** could be prepared in one pot with acceptable yields. At the meantime, a small part of starting materials diester **7** generated from the coupling could also be recycled. This approach thus directly provided two main short oligomers in one reaction and avoided nasty monohydrolysis of diester **7**. The desired heptamer **1** was successfully achieved in moderate yield by the coupling reaction between trimeric diamine and dimeric acid chloride.

2.2. Solid state studies

Single crystal X-ray diffraction provided detailed information about the double helical structures of heptamer **1** (Fig. 1 and S1). Yellow crystals of heptamer **1** suitable for crystallographic analysis were obtained upon diffusion of hexane into $C_2H_4Cl_2$ and chlorobenzene solution, respectively. Both crystal structures displayed a very similar double helical architecture (Section 4.3), which is unexpectedly different from that of oligoamides of pyridine, whose double helical structure possesses a C_2-symmetry axis.[5] In the present double helices, each strand is shifted by one aromatic ring, leading to that the diazaanthracene units in one strand and the fluorobenzene units in the other alternately stack onto each other. That is, each diazaanthracene unit in one strand was sandwiched between the two fluorobenzene units in the other strand and vice versa (Fig. 1). The global and extensive interstrand aromatic π–π stackings have been achieved as a result of such a slippage. This stacking pattern is likely due to the strong interactions between the electron-rich aminobenzene moiety and the electron-deficient diazaanthracence unit and partly due to the large surface of the fused aromatic units. All the fluorine atoms, amide protons, and diazaanthracene nitrogen atoms of the sequences point to the helical hollow cavity, and participate in the formation of a strong three-center F···HN and N···HN hydrogen bonding, which are one of main driven forces inducing the strand to adopt a helical structure. The double helical pitch is 7 Å, which is identical to that of all other double helices, and nearly four monomeric units are needed for one turn. However, the diameter of the double helices and arylamide torsions angles differ essentially. The inner diameter of the helix $(1)_2$ is about 5.4 Å, which is obviously larger than that of pyridine carboxamide oligomers. The tilt angle of the strand in the double helix $(1)_2$ is about 13° (Fig. S2), which is significantly smaller than that of the pyridine carboxamide oligomers (43°) and the pyridine carboxamide oligomers with a large unit in the middle of sequence (28°).[5] Hence, extensive interstrand interactions, enlarged diameter, and lower torsion angles render heptamer **1** readily to hybridize into a highly stable double helix based on spring-like extension mechanism.

2.3. Solution studies

The double helical structure of oligomer **1** was further confirmed by ^{1}H NMR, NOESY, and UV/vis spectra in solution. The ^{1}H NMR spectra of dimer and trimer in $CDCl_3$ show the sharp signal peaks of amide protons at low field (signals at 10–12 ppm) (Fig. 2 (a) and (b)), suggestive of the formation of intramolecular hydrogen bonding. However, the chemical shifts of amide and aromatic proton of heptamer **1** displays an obvious upfield shift compared to those of dimer and trimer (Fig. 2 (c)), in particular, the chemical shift of N*H*Boc shows about a shift of 1.2 ppm from 6.8 ppm to 5.6 ppm. The data imply that signals of heptamer were significantly



Scheme 1. Reagents and conditions: (a) di-*tert*-butyl-dicarbonate, dioxane, 80 °C, 4 days; (b) H_2, Pd/C, EtOAc, 8 h; (c) NaOH, THF/water, rt, 2 h; (d) 1-chloro-*N*,*N*,2-trimethylpropenylamine, DCM, rt, 10 h; (e) DIEA, DCM, rt, 6 h, then methanol; (f) NaOH, THF/water, rt, 4 h, then 1-chloro-*N*,*N*,2-trimethylpropenylamine, DCM, rt, 2 h; (g) TFA/DCM, rt, 2 h. (h) DIEA, DCM, rt, 10 h.

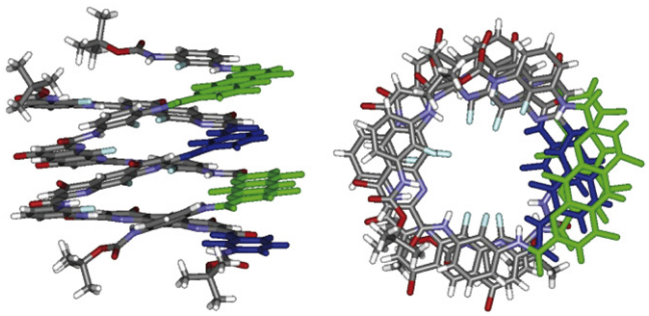


Fig. 1. Side view and top view of the crystal structures of heptamer **1** (crystals grown from $C_2H_2Cl_4$/hexane). The benzene and 1,7-diazaanthrancence moieties are labeled in deep blue and green, respectively. Isobutoxy side chains, hydrogen atoms, and solvent molecules are removed for clarity.

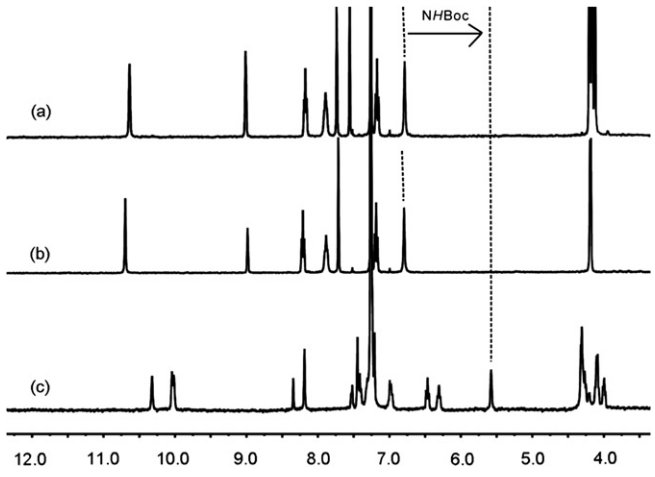


Fig. 2. The part of ^{1}H NMR spectra (400 MHz, $CDCl_3$, 1 mM, 20 °C) of (a) dimer **2**, (b) trimer **3**, (c) heptamer **1**.

shielded by aromatic π–π stacking either from single helix or double helix. Moreover, one set of signals observed for heptamer **1** hints at the existence of only one species in solution. By combining with the crystal data, we therefore can conclude that heptamer **1** prevails as a double helical conformation in solution.

The ROESY experiment was carried out to provide additional evidence to support the formation of the double helices. As shown in Fig. 3, the ROESY correlations observed between fluorobenzene and the isobutyl groups of the fused ring aromatic units reveal that fluorobenzene rings overlap with the 1,7-diazaanthracene rings, in agreement with crystal data. Furthermore, cross peaks were also found between amide protons of Boc groups and isobutyl groups. These contracts sufficiently confirm that the heptamer presents double helical conformation in solution. Given that **1** adopts a single helical structure, fluorobenzene rings would only overlap with other benzene units in the sequence but never with the 1,7-diazaanthracene moieties (Fig. S3). Finally, the formation of double helix in solution was also supported by ESI-MS that displays a doubly charged species $[2M+2H]^{+2}$ (Fig. S4).

In order to determine the dimerization constant K_{dim} of **1**, we performed ^{1}H NMR experiments in different solvents including the apolar solvents $CDCl_3$ and $C_2D_2Cl_4$ and polar solvent pyridine-d_5, a known solvent able to strongly weaken the hybridization of these oligomers. In all solvents, only one set of signals was detected at the concentration of 1 mM so we are unable to extract the dimerization constant from these NMR data (Fig. S5). Hence, to quantify K_{dim}, double helices must be dissociated to some extent so as to produce measurable parameters. Dilution and heating are two efficient approaches to dissociate double helices.[11] The UV/vis variable concentration experiments were carried out in $CHCl_3$ and pyridine (Fig. S6 and S7). The data showed that Lambert–Beer law was complied strictly even when the concentration was decreased to 0.5 μm. Neither hypochromism nor bathochromic shift was observed, suggesting that the double helical structure is rather robust with the K_{dim} value over 10^7 L mol^{-1} in chloroform and pyridine at rt, respectively. This phenomenon is sharply different from the case

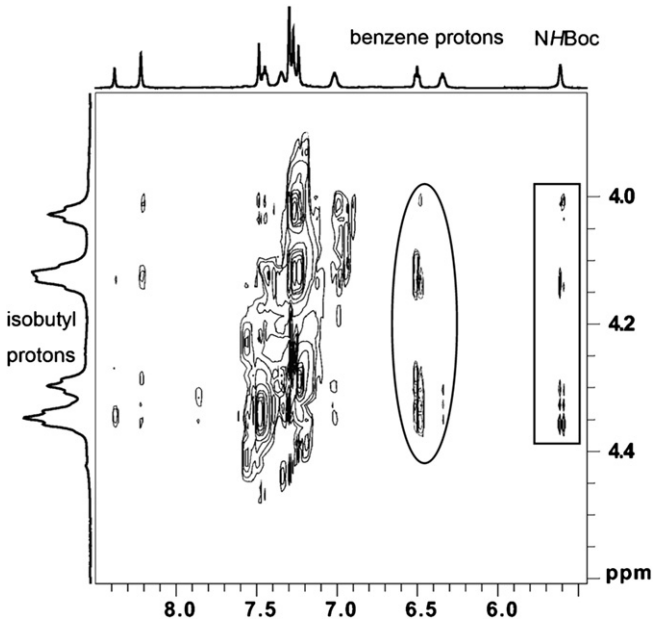


Fig. 3. Partial ROESY spectrum (600 MHz, $CDCl_3$, 1 mM, 20 °C) of heptamer **1**. Correlations observed between protons of the isobutyl groups and fluorobenzene and amide protons of Boc groups are labeled in ellipse and rectangle, respectively.

of pyridine carboxamide heptamer with an anthracene in the center, whose dimerization constant K_{dim} is 6.5×10^5 L mol^{-1} in pyridine at 25 °C.[5] Upon heating the solution of **1** (1 mM) in $C_2D_2Cl_4$ from 20 to 100 °C, the ^{1}H NMR spectrum revealed the emergence of a second set of signals at lower field (Fig. 4) indicative of the presence of the single helix of heptamer **1**. The proportions between these two sets of signals varied with temperatures, but no coalescence was observed. Integrating the two proportions of signals allowed us to estimate the dimerization constant $K_{dim}=1.7\times10^4$ L mol^{-1} at 80 °C and 7.9×10^3 L mol^{-1} at 100 °C in $C_2D_2Cl_4$, respectively.

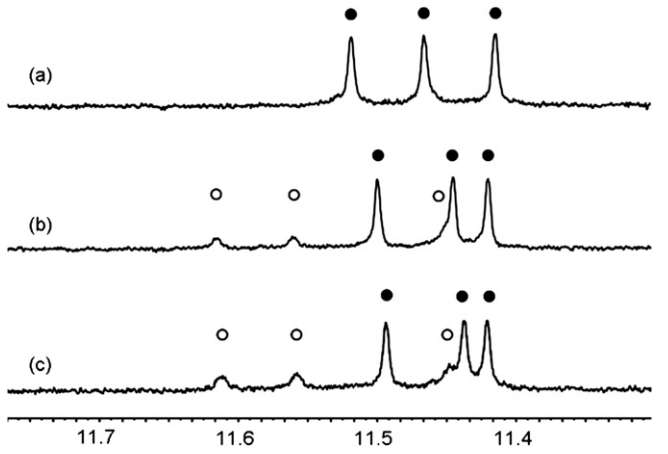


Fig. 4. Part of the 300 MHz ^{1}H NMR spectra in 1 mM $C_2D_2Cl_4$ solution showing amide resonances of heptamer **1** upon changing temperature: (a) 20 °C; (b) 80 °C; (c) 100 °C. Increasing the temperature leads to the onset of a new species in slow exchange on the NMR timescale. Signals belonging to the single and double helix are, respectively, marked with white and black circles.

3. Conclusion

We demonstrated that the stability of the double helices of aromatic oligoamides could be significantly enhanced by using a few of fused ring aromatic units in the sequences. Such enhancement mainly originates from the unique properties of the fused ring aromatic unit including large surface and size that lower the enthalpic cost of spring-like extension during the hybridization. It was expected that arylamide comprised of more or full fused ring aromatic units would display more stable double helices that is of great interest in constructing supramolecular polymers with highly stable helical structures by hybridization.

4. Experimental section

4.1. General procedure and materials

All coupling reactions were carried out under a dry nitrogen atmosphere. Materials were obtained from commercial suppliers and used without further purification unless otherwise specified. Dry dichloromethane (DCM), chloroform ($CHCl_3$), and diisopropylethylamine (DIPEA) were distilled from calcium hydride (CaH_2) prior to use. NMR spectra were recorded on Bruker AVANCE 600 (600 MHz), Bruker AVANCE 400 (400 MHz), and Bruker DMX 300 (300 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm, δ) using residual solvent protons as internal standards (chloroform: δ 7.26 ppm; tetrachloroethane: δ 6.00 ppm; DMSO: δ 2.50 ppm; pyridine: δ 8.74 ppm). EI, ESI mass spectra and MALDI-TOF were obtained on GCT, LC-MS 2010, Bruker Apex IV FTMS, and Autotlex III spectrometers, respectively.

4.2. Synthesis

*4.2.1. tert-Butyl (2-fluoro-3-nitrophenyl)carbamate (**5**).* A solution of 2-fluoro-3-nitroaniline[14] (0.24 g, 1.5 mmol) in dioxane (10 mL) containing di-*tert*-butyl-dicarbonate (1.0 g, 4.6 mmol) was heated at 60 °C for 3 days. The solvent was removed in vacuo, and the residue was purified by flash chromatography (SiO_2) eluting with hexane/CH_2Cl_2 from 100:10 to 100:50 vol/vol to afford the pure product (0.31 g, 80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.48 (t, J=9.6 Hz, 1H), 7.69–7.63 (m, 1H), 7.52 (t, J=2.4 Hz, 1H), 6.86 (br, 1H), 1.54 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.1, 146.6, 144.0, 137.4, 137.4, 129.5, 129.5, 125.1, 124.3, 124.3, 118.6, 118.5, 82.2, 28.3. MS (ESI): 279.1 $[M+Na]^+$ (calcd for $C_{11}H_{13}FN_2O_4Na$, 279.08).

*4.2.2. tert-Butyl (3-amino-2-fluorophenyl)carbamate (**6**).* Compound **5** (0.24 g, 0.94 mmol) was dissolved in EtOAc (20 mL), and of 10% Pd/C (25 mg) was added. The reaction mixture was stirred for 6 h under hydrogen at atmospheric pressure. After filtration through Celite and concentration, the residual oil was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2 to obtain product **6** as white solid (0.18 g, 85% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45 (t, J=6.4 Hz, 1H), 6.89–6.85 (m, 1H), 6.64 (br, 1H), 6.48–6.43 (m, 1H), 3.41 (br, 1H), 1.52 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.5, 143.4, 140.2, 134.3, 134.1, 127.2, 127.1, 124.3, 124.3, 111.0, 109.7, 80.9, 28.4. MS (ESI): 249.2 $[M+Na]^+$ (calcd for $C_{11}H_{15}FN_2O_2Na$, 249.10).

*4.2.3. Dimer (**2**) and trimer (**3**).* Diacid **8** (0.86 g, 2.0 mmol) was suspended in anhydrous $CHCl_3$ (10 mL). 1-Chloro-*N*,*N*,2-trimethylpropenylamine (0.53 mL, 2.0 equiv) was added and the reaction was allowed to stir at rt for 3 h. The reaction mixture remains a suspension, but the reaction does work under these conditions. The solvent and excess reagents were removed under vacuum and the residue was dried under vacuum for at least 2 h to yield acid chloride as a yellow-orange solid. To a solution of the freshly prepared diacid chloride in $CHCl_3$ (10 mL) was added dropwise a mixture solution of monoamine **6** (0.22 g, 1.0 mmol) and distilled DIPEA (0.68 mL, 4.0 mmol) in dry $CHCl_3$ (10 mL) at rt. Then, 1 mL MeOH was added. After 1 h stirring, the solution mixture was evaporated and the product was purified by flash

chromatography (SiO_2) eluting with CH_2Cl_2/EtOAc from 100:1 to 100:10 vol/vol to obtain **2** as a yellowish solid (0.39 g, 36% yield), and **3** as a yellowish solid (0.34 g, 32% yield). Meantime, starting materials **7** could be recycled (0.13 g, 12% yield). Dimer **2**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.65 (s, 1H), 9.01 (s, 1H), 8.19 (t, J=6.4 Hz, 1H), 7.89 (s, 1H), 7.74 (s, 1H), 7.55 (s, 1H), 7.19 (t, J=6.4 Hz, 1H), 6.79 (s, 1H), 4.21 (d, J=6.4 Hz, 2H), 4.17 (d, J=6.4 Hz, 2H), 4.13 (s, 3H), 2.41–2.35 (m, 2H), 1.56 (s, 9H), 1.21–1.19 (m, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.0, 163.7, 163.3, 161.8, 155.0, 152.8, 152.4, 152.3, 151.4, 144.1, 141.7, 136.2, 136.1, 135.1, 135.0, 127.1, 127.0, 126.0, 125.9, 124.5, 124.5, 122.4, 122.0, 115.3, 114.8, 111.1, 111.0, 99.6, 97.3, 81.3, 75.7, 75.5, 53.8, 28.4, 28.5, 28.3, 19.2. MS (MALDI-TOF): 653.2 $[M+H]^+$ (calcd for $C_{34}H_{39}F_2N_4O_7$, 653.28); 675.2 $[M+Na]^+$ (calcd for $C_{34}H_{38}F_2N_4O_7Na$, 675.26). Trimer **3**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.54 (s, 2H), 8.67 (s, 1H), 8.21 (t, J=6.4 Hz, 2H), 7.85 (s, 2H), 7.51 (s, 2H), 7.17 (t, J=6.4 Hz, 2H), 6.83 (s, 2H), 4.05 (d, J=6.4 Hz, 4H), 2.35–2.28 (m, 2H), 1.57 (s, 18H), 1.18 (d, J=6.6 Hz, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.6, 161.6, 152.6, 152.5, 144.1, 141.7, 134.9, 134.8, 127.0, 127.0, 126.2, 126.1, 124.6, 124.6, 121.9, 115.4, 114.5, 111.0, 110.9, 96.9, 81.3, 75.5, 28.4, 28.3, 19.2. MS (MALDI-TOF): 847.3 $[M+H]^+$ (calcd for $C_{44}H_{50}F_3N_6O_8$, 847.36); 869.3 $[M+Na]^+$ (calcd for $C_{44}H_{49}F_3N_6O_8Na$, 869.35).

*4.2.4. Heptamer (**1**).* Trimer **3** (0.42 g 0.5 mmol) was dissolved in CH_2Cl_2 (10 mL), and excess TFA (5 mL) was added. The mixture was stirred at rt for 3 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (20 mL), washed with saturated $NaHCO_3$, dried over Na_2SO_4, and then evaporated to give trimer diamine as a yellow solid. It was dried in vacuo, and used without further purification. Separately, dimer **2** (0.65 g, 1.0 mmol) was dissolved in a mixture of THF (50 mL) and H_2O (5 mL). NaOH (0.1 g, 2.5 mmol) was added, and the solution was stirred at rt for 5 h. The solution was neutralized with 1 N HCl to pH=4–5, then concentrated under reduced pressure to remove THF. H_2O (30 mL) was added to the residue. The aqueous phase was extracted with CH_2Cl_2 (3×50 mL). The combined organic phases were dried over Na_2SO_4 and then evaporated to give the corresponding dimer acid as a yellowish solid. It was dried in vacuo, and then dissolved in CH_2Cl_2 (10 mL). To this solution was added 1-chloro-*N*,*N*,2-trimethylpropenylamine (0.26 g, 2.0 mmol). The reaction mixture was stirred at rt for 2 h resulting in a homogeneous solution, then evaporated to provide the corresponding dimer acid chloride. To a solution of the trimer diamine in CH_2Cl_2 (20 mL) containing DIPEA (0.7 mL, 4.0 mmol) was added a solution of dimer acid chloride in CH_2Cl_2 (10 mL) via cannula. The reaction mixture was stirred at rt overnight. The solution was evaporated and the product was purified by flash chromatography (SiO_2) eluting with CH_2Cl_2/EtOAc from 100:5 to 100:20 vol/vol to obtain **1** as a yellowish solid (0.77 g, 82% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.32 (s, 2H), 10.04 (s, 2H), 10.01 (s, 2H), 8.34 (s, 1H), 8.18 (s, 2H), 7.44–7.20 (m, 12H), 6.99 (t, J=6.9 Hz, 2H), 6.49 (t, J=8.0 Hz, 2H), 6.32 (t, J=7.8 Hz, 2H), 5.58 (s, 2H), 4.31–3.97 (m, 12H), 2.54–2.31 (m, 6H), 1.41–1.23 (m, 36H), 1.01 (s, 18H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.6, 163.3 163.2, 161.1, 161.0, 160.8, 154.0, 152.0, 151.9, 151.8, 151.6, 151.5, 151.3, 142.6, 142.1, 140.1, 139.7, 134.9, 134.8, 134.5, 134.4, 125.7, 125.7, 125.2, 125.2, 123.3, 122.9, 121.6, 121.3, 121.2, 113.3, 113.0, 112.9, 112.6, 111.0, 110.9, 110.7, 110.6, 96.7, 96.6, 96.4, 80.7, 75.3, 75.2, 28.6, 28.5, 28.4, 27.7, 19.5, 19.5, 19.4, 19.4, 19.3. HRMS (ESI): 1888.73602 $[2M+2H]^{2+}$ (calcd for $C_{100}H_{102}F_7N_{14}O_{16}$, 1887.74865).

4.3. Single crystal X-ray diffraction

The data for crystal structures of compound **1** have been collected on a Rigaku MM07 HF rotating anode at the Mo Kα wavelength. The system features the micromax microfocus X-ray source with the Saturn 724 HG CCD detector combined with the AFC-Kappa goniometer and the osmic mirrors Varimax® HF optics. The system is driven by the CrystalClear[15] suite, which was also used for the unit cells determinations, the integration, scaling, and absorption correction of the raw data. All the structures have been solved by direct methods with SHELXD and refined by full-matrix least-squares methods using SHELXL.[16] The WinGX software was used for modeling.[17] It has to be noticed that all the crystals described below contain a large percentage of disordered solvent molecules and very few of them could be modeled in the Fourier difference density maps. High flux X-ray beams on small crystals with high solvent contents can explain the modest quality of the refinement statistics reported in this study.

Information concerning the crystallographic data collection and structure refinement of **1**: (a) crystallization solvent: hexane/1,2-dichloroethane, formula $C_{118}H_{137}Cl_{12}F_7N_{14}O_{16}$, Mw=2565.82, crystal size 0.2×0.2×0.2 mm^3, T=113(2) K, triclinic, space group $P-1$, a=22.924(5) Å, b=23.927(5) Å, c=27.624(6) Å, α=111.57(3)°, β=91.20(3)°, γ=111.53(3)°, V=12,893(4) Å^3, Z=8, ρ_{calcd}=1.322 g cm^{-3}; μ=0.333 mm^{-1}, unique data 46,843, parameters 2972, GOF=1.296, $R1$=0.1669, $wR2$=0.3041 for data ($I>2\sigma$ (I)), CCDC 846724; (b) crystallization solvent: hexane/chlorobenzene, formula $C_{124}H_{120}Cl_4F_7N_{14}O_{16}$, Mw=2333.76, crystal size 0.3×0.1×0.2 mm^3, T=113(2) K, triclinic, space group $P-1$, a=21.404(4) Å, b=21.827(4) Å, c=31.385(6) Å, α=94.18(3)°, β=108.49(3)°, γ=111.08(3)°, V=12,682(4) Å^3, Z=4, ρ_{calcd}=1.136 g cm^{-3}; μ=0.165 mm^{-1}, unique data 45,801, parameters 2678, GOF=1.071, $R1$=0.1795, $wR2$=0.3138 for data ($I>2\sigma$ (I)), CCDC 846725.

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Supplementary data

Supplementary data include experimental procedures, UV/vis, X-ray crystallography tables, high resolution ESI mass spectrum, and NMR spectra. Supplementary data associate with this article can be found at doi:10.1016/j.tet.2011.11.081.

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