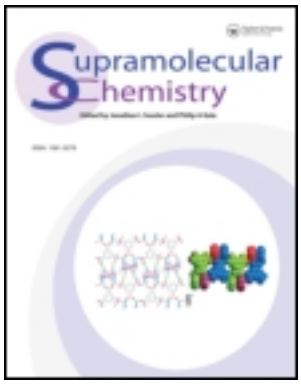

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Naphthalenediimide dimers and trimers form self-assembling hydrogen-bonded nanotubes of enhanced stability

John-Carl Olsen [a], Nora A. Batchelder [b], Julia H. Raney [c] & David E. Hansen [c d e]

[a] School of Sciences, Indiana University Kokomo, Kokomo, IN, 46904, USA

[b] Department of Chemistry, Amherst College, Amherst, MA, 01002, USA

[c] Keck Science Department, Claremont McKenna College, 925 N. Mills Avenue, Claremont, CA, 91711, USA

[d] Pitzer College, Claremont, CA, 91711, USA

[e] Scripps College, Claremont, CA, 91711, USA

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Naphthalenediimide dimers and trimers form self-assembling hydrogen-bonded nanotubes of enhanced stability

John-Carl Olsen[a], Nora A. Batchelder[b], Julia H. Raney[c] and David E. Hansen[c,d,e]*

[a]*School of Sciences, Indiana University Kokomo, Kokomo, IN 46904, USA;* [b]*Department of Chemistry, Amherst College, Amherst, MA 01002, USA;* [c]*Keck Science Department, 925 N. Mills Avenue, Claremont McKenna College, Claremont, CA 91711, USA;* [d]*Pitzer College, Claremont, CA 91711, USA;* [e]*Scripps College, Claremont, CA 91711, USA*

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Covalent linkage of amino acid-functionalised naphthalenediimides (NDIs) produced a dimer and a trimer that form helical, hydrogen-bonded nanotubes in $CHCl_3$ solutions and that are more resistant than an analogous monomer to the hydrogen-bond disrupting effects of tetrahydrofuran, methanol and heat.

Keywords: organic nanotubes; naphthalenediimide; dimer; trimer; solvophobic

Introduction

Given that their 'inherent geometric features, notably defined inner and outer surfaces as well as termini, give rise to a controlled spatial segregation' (*1*), organic nanotubes provide an active area of enquiry in supramolecular chemistry, and systems based on peptides, porphyrins, nucleobases and a variety of other small organic molecules have been described (*2–6*). Recently, the Sanders group (*7*) reported that amino acid-functionalised naphthalenediimide (NDI) monomers form helical hydrogen-bonded nanotubes in solvents of medium polarity and in the solid state. Appealing features of this remarkable new system include the ease of monomer synthesis (*8*), the toleration of different amino acid side chains (*7*, *9*, *10*) and the inclusion of various guest molecules, such as C_{60}, within the central pore of the nanotubes (*11–13*). In addition, the extent of nanotube formation is readily assayed by circular dichroism (CD) spectroscopy (*14–16*).

The nanotube architecture formed from NDI monomers derivatised with L-amino acids is depicted in Figure 1(a) (derived from a crystal structure published by the Sanders group (*7*)). Three monomers constitute one turn of the helix, and adjacent monomers (i and $i + 1$) are connected by hydrogen bonds between carboxylic acid groups. In addition, C—H···O hydrogen bonds between monomers four steps apart (i and $i + 3$) reinforce the assembly in the solid state. (These interactions, although weak, presumably provide the driving force for the formation of the nanotubes in solution – otherwise entropically more favourable 'random coils' would likely form, with NDI subunits only linked by the hydrogen bonds between carboxylic acid groups.) The naphthalene cores of the monomers form the walls of the nanotube, which are oriented parallel to its long axis. The amino acid side chains project out from the nanotube walls, and in our design we focused on the use of these side chains as the handles for the covalent linkage of NDI subunits.

Results and discussion

To probe further the versatility of the Sanders system, we have studied the properties of a dimer and a trimer formed by appropriate covalent linkage of NDI subunits. In particular, we employed molecular mechanics studies to explore potential covalent linkers between NDI monomer side chains separated by one turn of the helix (i and $i + 3$), and as shown in Figure 1(b), a terephthalic diester bridge through serine side chains appeared to be an effective modification. Dimer **4** and trimer **6** were thus synthesised using this linker, and the analogous monomer **2** was synthesised for use as a positive control (Figure 2 – also shown are the *t*-butyl esters **1**, **3** and **5**, the synthetic precursors to NDI derivatives **2**, **4** and **6**, respectively). We report here that dimer **4** and trimer **6** indeed form nanotubes in solution and that these nanotubes are significantly more resistant to THF, methanol and heat than those formed by monomer **2**.

The syntheses of NDI derivatives **2**, **4** and **6** relied on the microwave-heating approach developed by the Sanders group (*8*), a method that allows for the efficient conversion of 1,4,5,8-naphthalenetetracarboxylic dianhydride (NDA) into symmetric and unsymmetric amino acid-functionalised NDIs. The unsymmetric NDI derivative prepared from L-Phe-*t*-butyl ester and L-Ser-*t*-butyl ester was the

*Corresponding author. Email: dhansen@keckscl.claremont.edu

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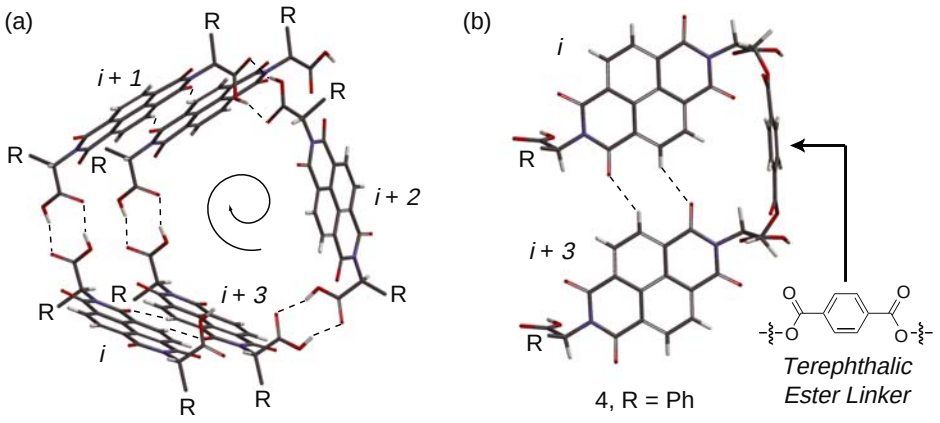


Figure 1. NDI nanotube segments. (a) An oblique view (modified from Ponnuswamy et al. (*14*)) composed of five NDI monomers that shows hydrogen bonds (black, dashed lines), the sense of the helix (black arrow) and the relative designation and orientation of several monomers (i, $i + 1$, $i + 2$ and $i + 3$). [Adapted with permission from Ponnuswamy, N.; Pantoş G.D.; Smulders, M.M.J.; Sanders, J.K.M. *J. Am. Chem. Soc.* 2012, *134*, 566–573; Copyright 2012, American Chemical Society.] (b) A molecular model of two adjacent NDI units (i and $i + 3$) of a nanotube, which are connected by a terephthalic ester linker.

key intermediate for the synthesis of the protected monomer **1** and protected dimer **3**. For the synthesis of protected trimer **5**, the symmetric bis(L-Ser-*t*-butyl ester) NDI derivative was also employed and served as the central subunit. Trifluoroacetic acid deprotection of derivatives **1**, **3** and **5** then yielded NDIs **2**, **4** and **6**, which were obtained from NDA in overall yields of 44%, 32% and 26%, respectively. (Complete synthetic details are provided below.)

As shown in Figure 3, the CD spectrum of monomer **2** at room temperature in neat $CHCl_3$ displays the signals characteristic of nanotube formation, with the most diagnostic being that at $\lambda = 383$ nm (the result of an induced Cotton effect from the NDI naphthalene core (*7*, *14*)). The spectrum of monomer **2** in the presence of 0.12% methanol lacks these signals, presumably due to disruption of the hydrogen bonds that hold the nanotube together. As expected, the CD spectrum for the NDI

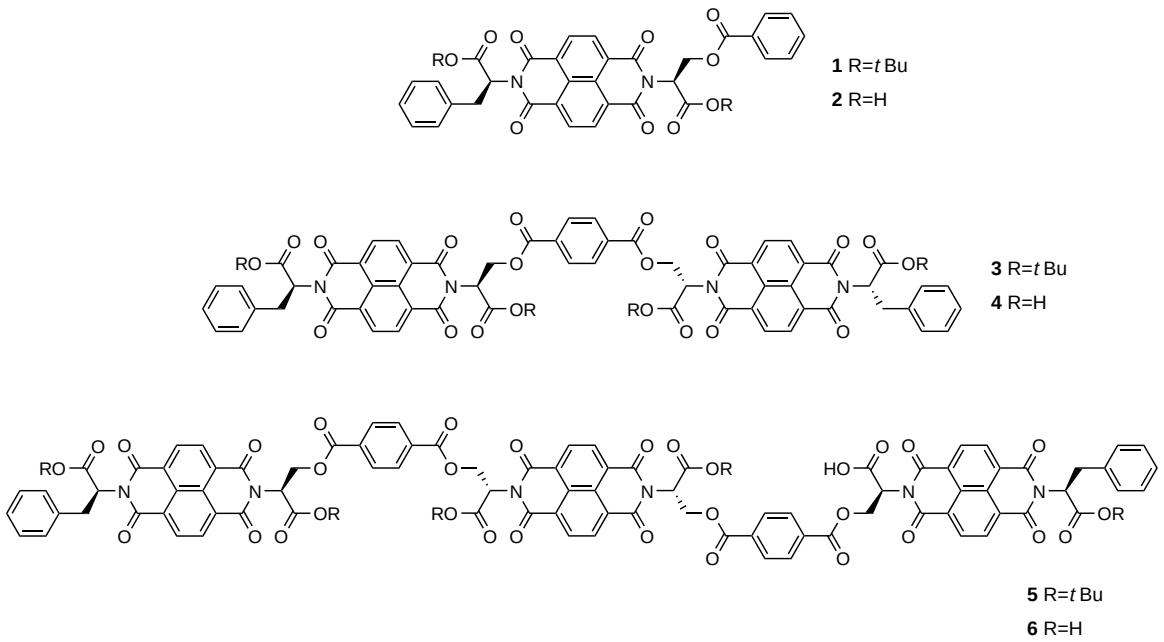


Figure 2. A homologous series of NDI acids – monomer **2**, dimer **4** and trimer **6** – and their corresponding *t*-butyl esters **1**, **3** and **5**.

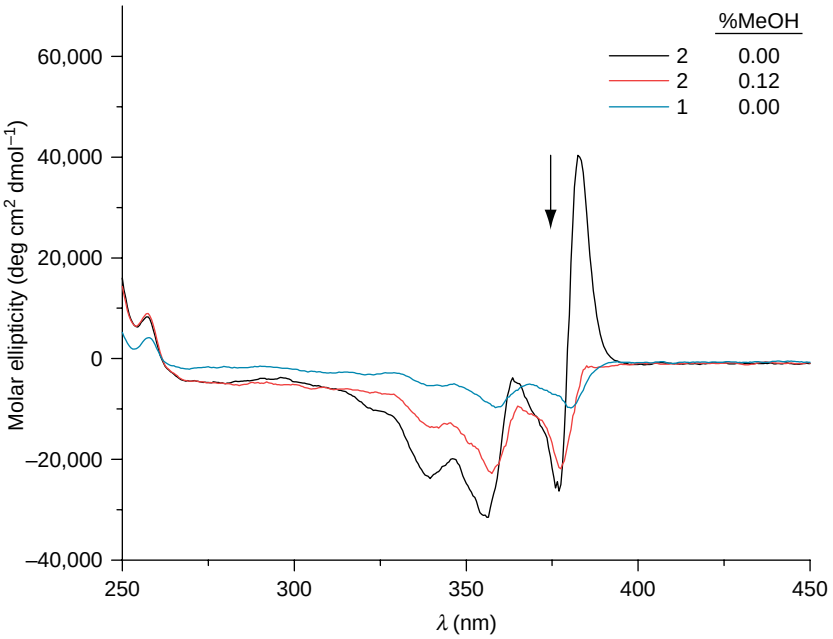


Figure 3. CD spectra of the methanol titration at room temperature (22°C) of NDI monomer **2** (initial concentration 6.9×10^{-5} M) in $CHCl_3$. For the CD spectrum of *t*-butyl-protected NDI monomer **1**, the concentration was 7.9×10^{-5} M. Molar ellipticities were calculated with respect to moles of NDI subunit.

monomer **1**, in which the essential hydrogen-bonding carboxylic acid functionalities are masked as *t*-butyl esters, also lacks the signals indicative of nanotube formation.

NDI dimer **4** is not soluble in pure $CHCl_3$, and thus, 0.5% THF in $CHCl_3$ was utilised to effect sample dissolution. Though the presence of 0.5% THF completely disrupts nanotube formation by monomer **2** (data not shown – see Supplementary Information, available online), dimer **4** forms nanotubes in this solvent system. In addition, these nanotubes are far more resistant to methanol than those formed from monomer **2** (Figure 4).

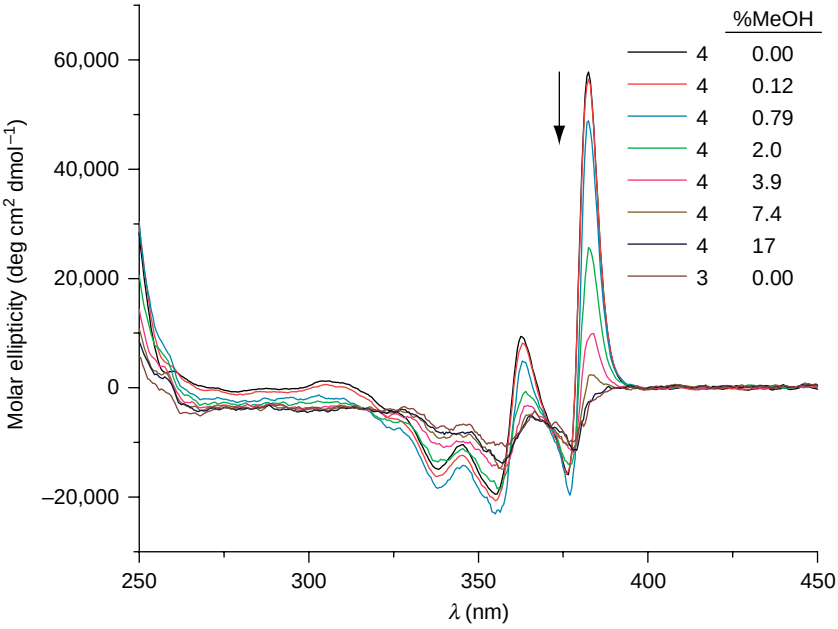


Figure 4. CD spectra of the methanol titration at room temperature (22°C) of NDI dimer **4** (initial concentration 4.6×10^{-5} M) in $CHCl_3$ containing 0.5% THF. The CD spectrum of *t*-butyl-protected NDI dimer **3** (4.3×10^{-5} M) was recorded in pure $CHCl_3$. Molar ellipticities were calculated with respect to moles of NDI subunit.

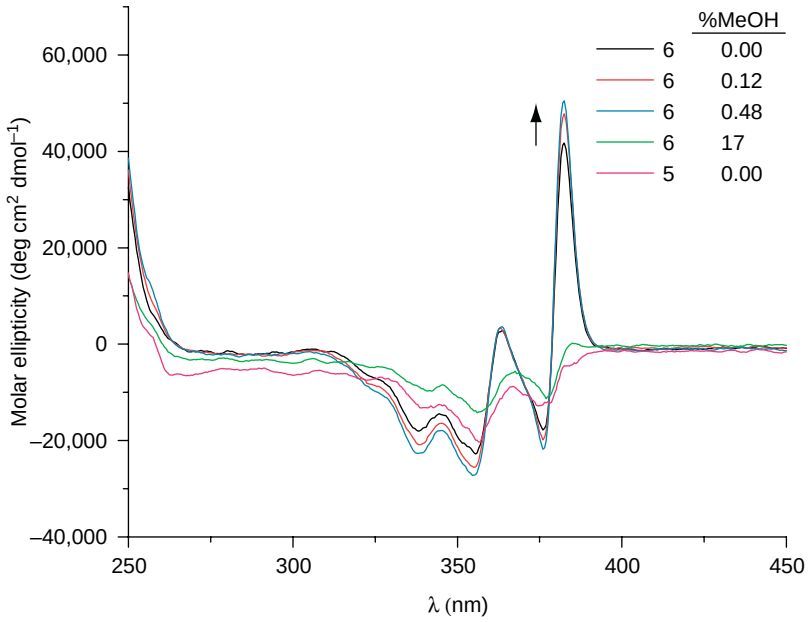


Figure 5. CD spectra of the methanol titration at room temperature (22°C) of NDI trimer **6** (initial concentration 1.7×10^{-5} M) in $CHCl_3$ containing 1.0% THF. The CD spectrum of *t*-butyl-protected NDI trimer **5** (2.3×10^{-5} M) was recorded in pure $CHCl_3$. Molar ellipticities were calculated with respect to moles of NDI subunit.

For example, in 0.12% methanol, the intensity of the signal at $\lambda = 383$ nm for dimer **4** decreases by only 1%. The addition of increasing amounts of methanol leads to further decreases in signal intensity, and in 17% methanol the nanotube signals completely disappear. As expected, the CD spectrum of dimer **4** in 17% methanol is similar to that of the *t*-butyl ester-protected dimer **3**.

To reproducibly obtain homogeneous solutions of trimer **6**, a further increase in THF concentration to 1.0% was required. Even in the presence of the 1.0% THF, however, trimer **6** forms nanotubes (Figure 5). Moreover, the intensity of the CD signal at $\lambda = 383$ nm *increases* upon small additions of methanol, reaching a maximum intensity at 0.48% methanol with a signal enhancement of 20%. These increases in intensity are indicative of a larger extent of nanotube formation (*14–16*). This result might be explained in terms of a competition between solvophobic (*1*, *12*) and hydrogen-bonding effects upon the addition of methanol, with the former favouring and the latter disfavouring nanotube formation. The nanotube assembly from trimer **6** may present less hydrophobic surface to the bulk solvent than the random, hydrogen-bonded polymer or than the completely dispersed and solvated trimers. The nanotube structure would thus be favoured in a solvent of higher polarity, as results from the addition of methanol. However, the ability of methanol to compete with the hydrogen bonds between NDI subunits in trimer **6** prevails at methanol concentrations $>0.48\%$, leading to the disruption of the nanotube structure. No increases in signal intensity are observed during the titration of the trimer with THF (data not shown – see Supplementary Information, available online), a result that suggests that the solvophobic effect seen with methanol may only occur with protic solvents.

Given the very small decrease noted above in the intensity of the $\lambda = 383$ nm signal for dimer **4** in 0.12% methanol, it is likely that the dimer also experiences a small stabilising solvophobic effect; however, for the dimer the disruption of the hydrogen bonding is a more dominant factor. The larger solvophobic effect for the trimer **6** may be due to the greater relative percentage of terephthalic ester linker present (the molar ratio of linker to NDI subunit is 0.67 for the trimer as compared with 0.50 for the dimer).

To probe further the stabilities of NDIs **2**, **4** and **6**, variable temperature CD data were collected (Figure 6). Monomer **2** was dissolved in neat $CHCl_3$, and dimer **4** and trimer **6** each in 1.0% THF in $CHCl_3$. Molar ellipticity was determined at $\lambda = 383$ nm in 1° increments from 5 to 55°C. The intensities at this wavelength for a solution of monomer **2** diminished far more rapidly than for either dimer **4** or trimer **6** and approached zero by 50°C, indicating essentially complete disruption of the nanotube structure at this temperature. In contrast, the intensities at $\lambda = 383$ nm for the solution of dimer **4** decreased by only 11% from 5 to 55°C, whereas for trimer **6** the decrease was 15% over this temperature range. In these experiments, the concentration of dimer **4** was 1.6 times that of trimer **6**, and thus, the concentrations of NDI subunit were approximately equal. Given the similar decreases in the $\lambda = 383$

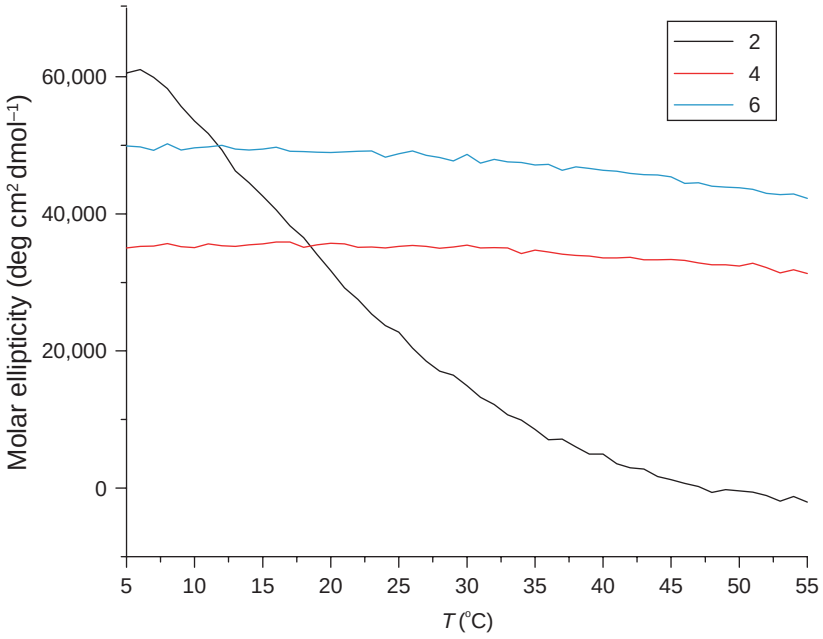


Figure 6. Variable temperature CD measurements of monomer **2** (6.9×10^{-5} M in $CHCl_3$, black trace), dimer **4** (2.2×10^{-5} M, 1.0% THF in $CHCl_3$, red trace) and trimer **6** (1.4×10^{-5} M, 1.0% THF in $CHCl_3$, blue trace). Signal intensity at $\lambda = 383$ nm was measured at 1° intervals from 5 to 55°C. Molar ellipticity was calculated with respect to moles of NDI subunit (colour online).

signal, the nanotubes formed by dimer **4** and trimer **6** appear to have comparable stabilities under these conditions. THF titrations of dimer **4** and trimer **6** (1.0–18% THF) also suggest that nanotubes formed from these two species – again at approximately equal NDI subunit concentrations – are comparably stable (data not shown – Supplementary Information, available online).

Conclusion

In conclusion, we have shown that NDI dimer **4** and trimer **6** form hydrogen-bonded nanotubes that, relative to the corresponding monomer **2**, resist the disrupting effects of THF, methanol and heat. Although additional studies (such as those recently reported by the Sanders group on their original system (*15*)) will be required to determine the underlying thermodynamic basis of these effects, the preorganisation of NDI subunits in dimer **4** and trimer **6** clearly leads to the formation of nanotubes of enhanced stability. Determination of the precise positioning of the terephthalic acid linker also awaits further work – though designed to bridge monomers four steps apart (i and $i + 3$), the linker could conceivably instead bridge adjacent monomers (i and $i + 1$), although our molecular mechanics studies suggest that this arrangement would be of higher energy; finally, the terephthalic ester might in fact serve as a cross-linker of arrays of nanotubes.

In the future, we wish to explore approaches that will lead to nanotubes of discrete length, in which both the NDI units are covalently linked and the terminal NDIs are modified to prevent further nanotube elongation (i.e. the nanotubes would be 'capped'). Our ultimate goal is to discover structural modifications that allow NDI-based nanotubes of discrete length to form in polar protic solvents.

Experimental details

Materials and methods

L-Phenylalanine-*t*-butyl ester hydrochloride (**8**) was purchased from Advanced Chem Tech (product number IF7427). L-Serine-*t*-butyl ester hydrochloride (**9**) was purchased from Indofine Chemical Company Inc. (product number 04-2437). Terephthalic acid monoallyl ester (**13**) was purchased from Chinglu Pharmaceutical Research LLC (product number A1160). Nuclear magnetic resonance (NMR) solvents were purchased from Aldrich and Cambridge Isotope Laboratories. Anhydrous $CHCl_3$ stabilised with amylene was purchased from Fisher (Acros product number 61028-1000). Flash chromatography was performed with silica gel 62 (60–200 mesh). Anhydrous tetrahydrofuran was obtained via elution through a solvent column drying system as described by Pangborn et al. (*17*). All other compounds were purchased from Aldrich, VWR or Fisher and used without further purification.

Microwave reactions were run in a Biotage Initiator microwave reactor in sealed 20-ml glass tubes capped with Teflon® septa. Reaction pressure was monitored by a non-invasive sensor within the lid of the reaction cavity that

measured the deformation of the Teflon® seal. Reaction temperature was monitored by an IR sensor. The temperatures indicated in the experimentals were the maximum temperatures reached during the reactions. The reaction times correspond to the total irradiation times. CD spectroscopy was performed using a JASCO J-715 spectropolarimeter. Sample solutions were measured in a quartz cuvette with a 1-cm path length. NMR spectra were obtained using a Bruker Avance III 500 MHz NMR spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane (TMS), and are referenced to TMS ($\delta = 0$ ppm) or, when TMS is absent, residual protium in the NMR solvent ($CDCl_3$: $\delta = 7.26$ ppm, DMSO-d_6: $\delta = 2.50$ ppm). Chemical shifts for carbon are reported in parts per million downfield from TMS, and are referenced to TMS ($\delta = 0$ ppm) or, when TMS is absent, to the carbon resonances of the solvent ($CDCl_3$: $\delta = 77.16$ ppm, DMSO-d_6: $\delta = 39.52$ ppm). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of a doublet, m = multiplet). Infrared spectroscopy was performed using a Thermo-Nicolet Avatar 370 FT-IR spectrometer. Mass spectrometric data were obtained at the University of California, Riverside High Resolution Mass Spectrometry Facility. The acronym LIFDI stands for 'liquid introduction, field desorption ionisation', which is a mass spectrometric technique described online at http://www.acif.ucr.edu/mspec/lifdi.html.

Molecular mechanics calculations were made using HyperChem Release 5.11 Pro for Windows (Hypercube, Inc.). The MM+ force field with the block-diagonal Newton–Raphson algorithm was employed, and all minimisations were terminated at an RMS gradient of 0.1 kcal/(Å mol) or less.

Synthetic details

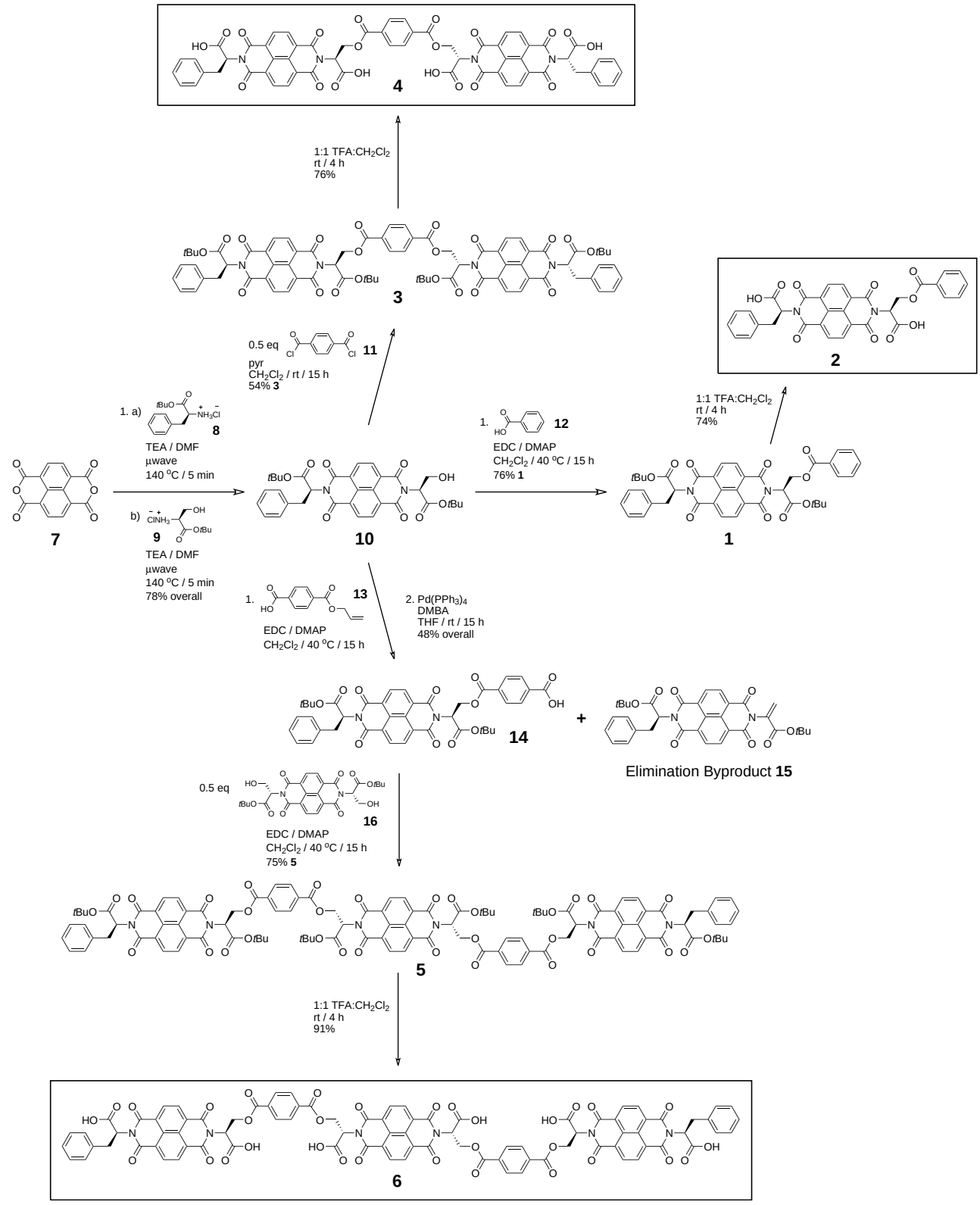
The synthetic routes to monomer **2**, dimer **4** and trimer **6** are outlined in Scheme 1.

*NDI monomer **10***

1,4,5,8-Naphthalenetetracarboxylic dianhydride (300 mg, 1.12 mmol), L-Phe-*t*-butyl ester hydrochloride (**8**) (289 mg, 1.12 mmol), dimethylformamide (15 ml) and triethylamine (0.312 ml, 2.24 mmol) were added in that order to a 20-ml pressure tube. The reaction mixture was sonicated for 30 min and then stirred and heated in a microwave reactor for 5 min at 140°C. After the reaction mixture had cooled to room temperature, L-Ser-*t*-butyl ester hydrochloride (**9**) (0.221 g, 1.12 mmol) and triethylamine (0.312 ml, 2.24 mmol) were added. The mixture was again stirred and heated in a microwave for 5 min at 140°C. After cooling, the solvent was evaporated. The residue was dissolved in dichloromethane (50 ml), transferred to a separatory funnel and rinsed with water (3 × 50 ml) and brine (50 ml). The organic layer was separated and dried over sodium sulphate. The product was adsorbed onto silica gel by evaporation, dry loaded onto a silica gel column and separated by flash chromatography with dichloromethane. Fractions containing product were combined; the solvent was evaporated and the product was placed under a high vacuum overnight to give NDI di-*t*-butyl ester **10** as a yellow solid (553 mg, 78%); m.p. 115–120°C (dec.); IR (KBr) 3534, 2978, 2937, 1739, 1709, 1672, 1344, 1248 and 1158 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.73$ (d, $J = 7.5$ Hz, 2H), 8.67 (d, $J = 7.5$ Hz, 2H), 7.15–7.04 (m, 5H), 5.93 (dd, $J = 10.5$, 5.5 Hz, 1H), 5.72 (t, $J = 6.5$ Hz, 1H), 4.39 (dd, $J = 11.5$, 6.5 Hz, 1 H), 4.02 (dd, $J = 6.5$, 12.0 Hz, 1 H), 3.67 (dd, $J = 14.5$, 5.5 Hz, 1 H), 3.49 (dd, $J = 14.5$, 10.5 Hz, 1 H), 2.647 (bs, 1H), 1.47 (s, 9 H), 1.46 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 168.0$, 167.7, 162.6, 162.2, 137.2, 131.4, 131.2, 129.1, 128.4, 126.8, 126.7, 126.6, 126.4, 126.3, 83.2, 82.5, 60.8, 55.7, 55.6, 34.8, 27.9 ppm; HRMS (ESI +): calcd for $C_{34}H_{34}N_2O_9Na$: 637.2157; found: 637.2151 $[M + Na]^+$.

*NDI monomer **14***

NDI di-*t*-butyl ester **10** (2.48 g, 4.03 mmol), terephthalic acid monoallyl ester (**13**) (831 mg, 4.03 mmol), EDC (850 mg, 4.43 mmol) and DMAP (0.492 mg, 4.03 mmol) were dissolved in dichloromethane (80 ml) and refluxed overnight at 40°C. The reaction mixture was partitioned between dichloromethane (300 ml) and water (300 ml). The organic layer was separated, washed with water (300 ml) and brine (300 ml) and dried over sodium sulphate. The solution was filtered through a plug of silica gel with hexanes:ethyl acetate (5:1). The solvent was evaporated, and the crude product, which contained the NDI alkene derivative **15** as an inseparable by-product, was dried overnight under a high vacuum. This product mixture (1.95 g), tetrakis(triphenylphosphine)palladium(0) (140 mg, 0.122 mmol) and dimethylbarbituric acid (398 mg, 2.55 mmol) were dissolved in THF (49 ml). The solution was stirred at room temperature for 4 h, adsorbed onto silica gel by evaporation and dry loaded onto a silica gel column. The product was separated by flash chromatography with hexanes followed by a mixture of hexanes, ethyl acetate and acetic acid (200:795:5). Fractions containing product were combined, the solvent was evaporated and the sample was placed under a high vacuum overnight to give terephthalic acid NDI half-ester **14** as a pale, yellow-green powder (1.29 g, 48% for two steps). m.p. 139–145°C (dec.); IR (KBr) cm^{-1} 3374.0, 3083.2, 2978.4, 2933.5, 1732.2, 1710.5, 1673.8 and



Scheme 1. Synthetic routes to NDIs **2**, **4** and **6**. DMBA, dimethylbarbituric acid; EDC, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.

1582.4 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.73$ (d, $J = 7.5$ Hz, 2H), 8.68 (d, $J = 7.5$ Hz, 2H), 8.05 (d, $J = 8.5$ Hz, 2H), 7.97 (d, $J = 8.0$ Hz, 2H), 7.15–7.04 (m, 5H), 6.10 (dd, $J = 9.3$, 4.2 Hz, 1H), 5.94 (dd, $J = 10.0$, 4.3 Hz, 1H), 5.21 (dd, $J = 11.7$, 4.3 Hz, 1H), 4.98 (dd, $J = 11.5$, 9.5 Hz, 1H), 3.67 (dd, $J = 14.5$, 5.5 Hz, 1H), 3.48 (dd, $J = 14.3$, 10.3 Hz, 1H), 1.50 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 170.5$, 168.0, 165.6, 165.3, 162.5, 162.2, 137.2, 134.1, 133.1, 131.4, 131.2, 130.1, 129.7, 129.1, 128.4, 126.9, 126.7, 126.6, 126.5, 126.2, 83.6, 82.6, 62.8, 55.6, 53.6, 34.8, 27.9 ppm; HRMS (LIFDI): calcd for $C_{33}H_{22}N_2O_{10}$: 762.2419; found: 762.2383 M^+.

*NDI monomer **16***

1,4,5,8-Naphthalenetetracarboxylic dianhydride (1.26 g, 4.7 mmol), L-Ser-*t*-butyl ester hydrochloride (**9**) (2.05 g, 10.4 mmol), dimethylformamide (15 ml) and triethylamine (2.62 ml, 18.8 mmol) were added to a 20-ml pressure tube. The reaction mixture was sonicated for 30 min and then stirred and heated in a microwave reactor for 8 min at 140°C. The reaction mixture was cooled to room temperature, and the solvent was evaporated. The residue was dissolved in dichloromethane (300 ml), transferred to a separatory funnel and rinsed with water (3 × 300 ml) and brine (300 ml). The organic layer was dried over sodium sulphate. After removal of the drying agent, the solution was adsorbed onto silica gel by evaporation. The sample was dry loaded onto a silica gel column, and the product was separated by flash chromatography with hexanes:ethyl acetate (2:1 → 1:1 → 1:2). Fractions containing product were combined, the solvent was evaporated and the sample was placed under a high vacuum overnight to give *t*-butyl-protected bis-serine NDI **16** as a yellow solid (2.09 g, 80%). m.p. 160–165°C (dec.); IR (KBr) 3508, 3085, 2978, 1739, 1708, 1670, 1582 and 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.78$ (s, 4H), 5.73 (t, $J = 6.5$ Hz, 2H), 4.41 (dd, $J = 11.5$, 6.5 Hz, 2H), 4.04 (dd, $J = 11.5$, 6.5 Hz, 2H), 2.76 (bs, 2H), 1.45 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 167.6$, 162.6, 131.4, 126.9, 126.5, 83.2, 60.7, 55.7, 27.9 ppm; HRMS (ESI +): calcd for $C_{28}H_{30}N_2O_{10}Na$: 577.1797; found: 577.1799 $[M + Na]^+$.

*NDI monomer **1***

NDI di-*t*-butyl ester **10** (200 mg, 0.325 mmol), benzoic acid (43.7 mg, 0.358 mmol), EDC 68.6 mg, 0.358 mmol) and DMAP (43.7 mg, 0.358 mmol) were dissolved in dichloromethane (10 ml) and refluxed at 40°C overnight. After cooling, the reaction mixture was partitioned between dichloromethane (50 ml) and 1 M HCl (aq.) (50 ml). The organic layer was separated and washed with water (50 ml) and brine (50 ml) and dried over sodium sulphate. The solution was decanted, and the sample was adsorbed onto silica gel by evaporation and dry loaded onto a silica gel column. The product was separated by flash chromatography with hexanes:ethyl acetate (5:1). Fractions containing product were combined, the solvent was evaporated and the sample was placed under a high vacuum overnight to give NDI di-*t*-butyl ester **1** as a pale, blue-green solid (183 mg, 76%). m.p. 105–109°C; IR (KBr) 3427, 3064, 2978, 2937, 1736, 1711 and 1673 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.73$ (d, $J = 7.5$ Hz, 2H), 8.67 (d, $J = 7.5$ Hz, 2H), 7.87 (d, $J = 7.5$ Hz, 2H), 7.49 (t, $J = 7.5$ Hz, 1H), 7.33 (m, $J = 7.5$ Hz, 2H), 7.14–7.04 (m, 5H), 6.11 (dd, $J = 9.5$, 4.5 Hz, 1H), 5.93 (dd, $J = 10.0$, 5.5 Hz, 1H), 5.15 (dd, $J = 12.0$, 4.0 Hz, 1H), 4.98 (dd, $J = 11.5$, 9.5 Hz, 1H), 3.67 (dd, $J = 14.5$, 5.5 Hz, 1H), 3.48 (dd, $J = 14.0$, 10.5 Hz, 1H), 1.50 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 167.9$, 166.2, 165.7, 162.5, 162.3, 137.2, 133.1, 131.4, 131.2, 129.6, 129.1, 128.37, 128.35, 126.9, 126.74, 126.65, 126.4, 126.3, 83.4, 82.5, 62.3, 55.6, 53.7, 34.8, 28.0 ppm; HRMS (LIFDI): calcd for $C_{41}H_{38}N_2O_{10}$: 718.2521; found: 718.2532 M^+.

*NDI monomer **2***

NDI di-*t*-butyl ester **1** (502 mg, 0.699 mmol), trifluoroacetic acid (14 ml) and dichloromethane (14 ml) were stirred at room temperature for 4 h. The solvent was evaporated, and the sample was placed under a high vacuum overnight to give NDI monomer **2** as a yellow powder (312 mg, 74%). m.p. 159–163°C; IR (KBr) 3491, 3202, 3087, 2939, 2589, 1709, 1673 and 1347 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 298 K): $\delta = 13.30$ (bs, 2H), 8.74 (d, $J = 7.5$ Hz, 2H), 8.69 (d, $J = 7.0$ Hz, 2H), 7.81 (d, $J = 6$ Hz, 2H), 7.58 (bs, 1H), 7.42 (bs, 2H), 7.19–7.04 (m, 5H), 6.09 (dd, $J = 8.0$, 4.5 Hz, 1H), 5.92 (dd, $J = 9.0$, 6.0 Hz, 1H), 5.10 (dd, $J = 11.2$, 3.8 Hz, 1H), 4.85 (t, $J = 10.0$ Hz, 1H), 3.63 (dd, $J = 13.7$, 5.2 Hz, 1H), 3.37 (dd, $J = 13.5$, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 171.2$, 169.3, 166.4, 163.3, 162.9, 138.6, 134.2, 132.2, 130.1, 130.0, 129.9, 129.5, 129.1, 127.3, 127.2, 126.9, 126.6, 63.2, 55.8, 55.5, 53.2, 35.2 ppm; HRMS (ESI +): calcd for $C_{33}H_{22}N_2O_{10}$: 606.1269; found: 606.1241 M^+.

*NDI dimer **3***

NDI di-*t*-butyl ester **10** (3.23 g, 5.26 mmol), terephthalyl chloride (0.534 g, 2.63 mmol) and DMAP (0.483 g, 3.95 mmol) were dissolved in dichloromethane (105 ml). Pyridine (0.466 ml, 5.78 mmol) was added, and the solution was stirred at room temperature for 48 h. The reaction mixture was adsorbed onto silica gel by

evaporation and dry loaded onto a silica gel column. The product was separated by flash chromatography with hexanes:ethyl acetate (5:1 → 3:1). Fractions containing product were combined; the solvent was evaporated, and the sample was placed under a high vacuum overnight to give NDI tetra-*t*-butyl ester **3** as a yellow solid (1.95 g, 54%). m.p. 156–160°C; IR (KBr) 3086, 2978, 2936, 1739, 1711, 1675 and 1247 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.72$ (d, $J = 7.5$ Hz, 4H), 8.68 (d, $J = 7.5$ Hz, 4H), 7.85 (s, 4H), 7.1–7.03 (m, 10H), 6.06 (dd, $J = 9.0$, 4.0 Hz, 2H), 5.94 (dd, $J = 10.4$, 5.5 Hz, 2H), 5.16 (dd, $J = 12.0$, 4.5 Hz, 2H), 4.95 (dd, $J = 11.5$, 9.3 Hz, 2H), 3.67 (dd, $J = 14.0$, 5.5 Hz, 2H), 3.48 (dd, $J = 14.5$, 10.5, 2H), 1.48 (s, 18H), 1.46 (s, 18H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 168.2$, 165.9, 165.6, 162.8, 162.5, 137.5, 133.8, 131.7, 131.5, 129.9, 129.4, 128.7, 127.2, 127.1, 126.9, 126.8, 126.4, 83.8, 82.8, 63.1, 55.9, 53.9, 35.1, 28.3 ppm; HRMS (ESI +): calcd for $C_{76}H_{70}N_4O_{20}Na$: 1381.4476; found: 1381.4442 $[M + Na]^+$.

*NDI dimer **4***

NDI tetra-*t*-butyl ester **3** (1.82 g, 1.34 mmol), triethylsilane (1.56 ml, 13.4 mmol), trifluoroacetic acid (27 ml) and dichloromethane (27 ml) were added to a flask and stirred at room temperature for 2 h. The solvent was evaporated, and the residue was triturated twice with dichloromethane and placed under a high vacuum overnight to give NDI dimer **4** as a yellow-green powder (1.17 g, 76%). m.p. 220–228°C; IR (KBr) 3522, 3085, 2940, 2602, 1709, 1670, 1581, 1348 and 1249 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 298 K): $\delta = 13.41$ (bs, 2H), 13.15 (bs, 2H), 8.68 (d, $J = 7.5$ Hz, 4H), 8.64 (d, $J = 7.5$ Hz, 4H), 7.80 (s, 4H), 7.13–6.96 (m, 10H), 6.01 (dd, $J = 8.0$, 4.5 Hz, 2H), 5.87 (dd, $J = 9.5$, 6.0 Hz, 2H), 5.05 (dd, $J = 11.5$, 9.0 Hz, 2H), 4.79 (dd, $J = 11.5$, 9.0 Hz, 2H), 3.57 (dd, $J = 14.2$, 5.3 Hz, 2H), 3.32 (dd, $J = 14.0$, 10.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): $\delta = 170.2$, 168.3, 164.7, 162.4, 162.0, 137.6, 133.2, 131.3, 129.3, 128.9, 128.1, 126.3, 126.05, 125.99, 125.6, 62.7, 54.9, 54.5, 52.2, 34.2 ppm; HRMS (ESI +): calcd for $C_{60}H_{38}N_4O_{20}Na$: 1157.1972; found: 1157.1960 $[M + Na]^+$.

*NDI trimer **5***

Terephthalic acid NDI half-ester **14** (500 mg, 0.813 mmol), *t*-butyl-protected bis-serine NDI **16** (138 mg, 0.312 mmol), EDC (240 mg, 1.25 mmol) and DMAP (38.1 mg, 13.7 mmol) were dissolved in dichloromethane (13.7 ml) and refluxed at 40°C overnight. After cooling, the reaction mixture was partitioned between dichloromethane (50 ml) and 1 M HCl (aq.) (50 ml). The organic layer was separated and washed with water (50 ml) and brine (50 ml) and dried over sodium sulphate. The solution was decanted, and the sample was adsorbed onto silica gel by evaporation and dry loaded onto a silica gel column. The product was separated by flash chromatography with hexanes:ethyl acetate (4:1 → 2:1). Fractions containing product were combined, the solvent was evaporated and the sample was placed under a high vacuum overnight to give NDI hexa-*t*-butyl ester **5** as a pale, blue-green solid (449 mg, 75%). m.p. 182–185°C; IR (KBr) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 298 K): $\delta = 8.71$–8.67 (m, 12H), 7.85 (s, 8H), 7.15–7.01 (m, 10H), 6.08–6.04 (m, 4H), 5.96–5.92 (dd, $J = 10.5$, 5.5 Hz, 2H), 5.19–5.14 (m, 4H), 4.99–4.92 (m, 4H), 3.66 (dd, $J = 14.0$, 5.5, 2H), 3.48 (dd, $J = 14.0$, 10.0 Hz, 2H), 1.48 (s, 36H), 1.46 (18H); ^{13}C NMR (125 MHz, DMSO-d_6, 298 K): $\delta = 167.9$, 165.55, 165.52, 165.3, 162.5, 162.4, 162.2, 137.3, 133.49, 133.45, 131.5, 131.4, 131.2, 129.6, 129.1, 128.3, 127.0, 126.9, 126.7, 126.6, 126.5, 126.4, 126.1, 83.5, 82.5, 62.85, 62.80, 55.6, 53.65, 53.61, 34.8, 27.9 ppm; HRMS (ESI +): calcd for $C_{112}H_{102}N_6O_{32}Na$: 2065.6431; found: 2065.6446 $[M + Na]^+$.

*NDI trimer **6***

NDI hexa-*t*-butyl ester **5** (193 mg, 0.106 mmol), trifluoroacetic acid (5 ml) and dichloromethane (5 ml) were stirred at room temperature for 4 h. The solvent was evaporated, and the residue was triturated with dichloromethane and placed under a high vacuum overnight to give **6** as a pale green powder (164 mg, 91%) m.p. 230–234°C (dec.); IR (KBr) 3516, 3085, 2940, 2606, 1709, 1673 and 1582 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 298 K): $\delta = 13.43$ (bs, 6H), 8.76–8.64 (m, 12H), 7.70–7.90 (m, 8H), 7.00–7.15 (m, 10H), 6.05–5.98 (m, 4H), 5.90–5.84 (m, 2H), 5.20–5.14 (m, 4H), 4.90–4.77 (m, 4H), 3.52–3.62 (m, 2H), 3.50–3.28 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6, 298 K): $\delta = 171.1$, 169.2, 165.51, 165.48, 163.29, 163.26, 162.9, 138.5, 134.1, 134.0, 132.2, 130.13, 130.08, 129.8, 129.0, 127.24, 127.19, 126.91, 126.88, 126.5, 63.6, 55.9, 55.4, 53.1, 35.1 ppm; HRMS (ESI −): calcd for $C_{88}H_{53}N_6O_{32}$: 1705.2710; found: 1705.2703 [M − H].

Supplementary material

^1H and ^{13}C NMR spectra for all new compounds are provided, as are CD spectra showing the effect of THF on nanotube formation by monomer **2**, dimer **4** and trimer **6**. The supplementary material is available with the online version of this paper at http://www.tandfonline.com/gsch.

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