Available online at www.sciencedirect.com

Tetrahedron Letters

Tetrahedron Letters 46 (2005) 5695–5698

Self-assembly of naphthalene diimides into cylindrical microstructures

Massimiliano Tomasulo,[a] David M. Naistat,[a] Andrew J. P. White,[b] David J. Williams[b] and Françisco M. Raymo[a,*]

[a]*Center for Supramolecular Science, Department of Chemistry, University of Miami, 1301 Memorial Drive, FL 33146-0431, USA*
[b]*Department of Chemistry, Imperial College London, South Kensington, London SW7 2AY, UK*

Received 8 June 2005; revised 16 June 2005; accepted 16 June 2005
Available online 5 July 2005

Abstract—We have designed two rod-shaped compounds each incorporating a naphthalene diimide core and two terminal carboxylic acids. Both molecules aggregate in aqueous solution and spontaneously organize into cylindrical microstructures on the surface of solid substrates. Presumably, hydrogen bonds between the carboxylic acid termini and hydrophobic contacts between the naphthalene diimide cores are mainly responsible for the formation of these supramolecular arrays. Indeed, extended stacks of molecules self-assemble with close contacts between their aromatic cores in single crystals grown from polar solvents.

Nature relies on the power of self-assembly to construct complex supramolecular architectures.[1] The double helix of DNA, the membrane of a living cell and the coat of tobacco mosaic virus are, perhaps, the most striking examples of self-assembly in action. These amazing supramolecular constructs are collections of molecular building blocks organized with remarkable precision by a multitude of weak, but cooperative, noncovalent bonds. In search of viable operating principles to mimic the mode of assembly and the fascinating structures of these biological systems, a number of strategies to ensure the spontaneous organization of supramolecular synthons into fibers, helices, layers, rods and tubes have been envisaged.[2] A particularly promising approach is based on the design of linear compounds with hydrophobic cores and hydrophilic ends. These molecules, often termed bolaamphiphiles,[2] associate into organized nanostructures in polar environments. Specifically, hydrogen bonds at the hydrophilic ends and van der Waals contacts at the hydrophobic cores guide the assembly of these compounds into supramolecular arrays. Generally, the hydrophilic termini are pairs of amino acids,[3–5] carbohydrates,[6] dendritic alcohols[7] or nucleobases[8] and the hydrophobic spacers between them are single aliphatic chains. The replacement of the aliphatic bridges with aromatic chromophores having large molar extinction coefficients and even emissive behaviour, however, can certainly facilitate the spectroscopic analysis of these supramolecular processes. Despite these obvious advantages, self-assembling nanostructures based on aromatic bolaamphiphiles are limited to few examples.[9–11] We have designed two rod-shaped molecules (**1** and **2** in Fig. 1) combining a fluorescent naphthalene diimide[12] core with terminal carboxylic acids. In this letter, we report the synthesis of these compounds, their self-assembly into organized microstructures and the crystal structure for one of the two molecules.

We have synthesized compounds **1** and **2** in a single step (Fig. 1) starting from 1,4,5,8-naphthalenetetracarboxylic dianhydride and either glycine or β-alanine. Indeed, the reaction of these precursors in aqueous environment affords the corresponding diimides **1** and **2** in yields of 62% and 41%, respectively, after crystallization from acetonitrile. Both compounds dissolve readily in sodium phosphate buffer (pH = 7.0) with concentrations up to 3.0 and 1.8 mM, respectively. The absorption spectra (***a*** in Fig. 2 and Fig. S1) of the resulting solutions show bands between 300 and 400 nm for the naphthalene diimide chromophore with a molar extinction coefficient of ca. 18 $mM^{-1}\,cm^{-1}$ at 362 nm. The concentration dependence of the absorbance at this particular wavelength,

---

Keywords: Bolaamphiphiles; Hydrogen bonding; Hydrophobic interactions; Naphthalene diimides; Self-assembly; Supramolecular arrays.

* Corresponding author. Tel.: +1 305 284 2639; fax: +1 305 284 4571; e-mail: fraymo@miami.edu

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.06.086

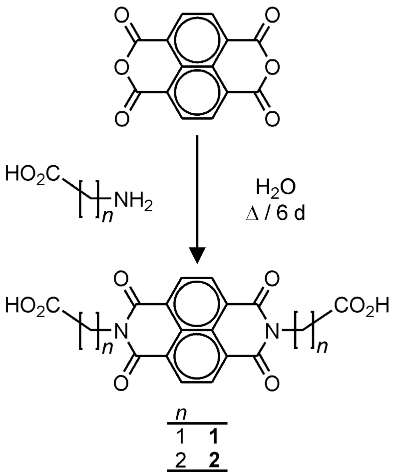


Figure 1. Synthesis of the naphthalene diimides **1** and **2**.

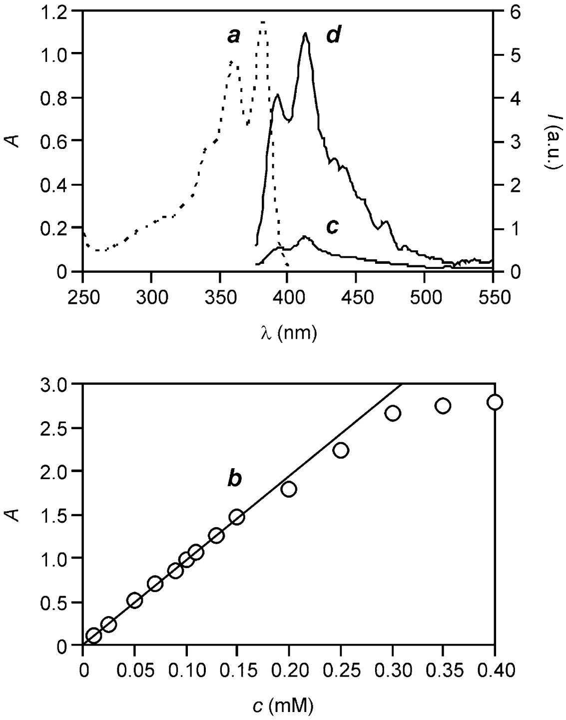


Figure 2. Absorption spectrum (***a***) of 1 (0.1 mM) in sodium phosphate buffer (pH = 7.0, 20 °C) and concentration dependence (***b***) of the absorbance at 362 nm. Emission spectra ($\lambda_{exc.}$ = 362 nm) of **1** (0.01 mM) in sodium phosphate buffer (pH = 7.0, 20 °C) recorded immediately after the preparation of the solution (***c***) and storage for 45 min (***d***).

however, deviates from linearity at concentrations greater than 0.15 mM for **1** (***b*** in Fig. 2) and 0.25 mM for **2** (***b*** in Fig. S1). Thus, the amphiphilic building blocks aggregate into supramolecular assemblies above these particular concentration thresholds. Consistently, the emission spectrum of **1** (***c*** in Fig. 2), recorded immediately after dilution from 1.0 to 0.01 mM, shows that the fluorescence of the naphthalene diimide core is almost completely suppressed. After 45 min, however, the emission spectrum (***d*** in Fig. 2) of the very same solution reveals clearly the characteristic fluorescence of the emissive core. This change in emission intensity indicates that the supramolecular assemblies present at a concentration of 1.0 mM survive the initial dilution to 0.01 mM, but dissociate gradually over the course of 45 min. Interestingly, the kinetics of dissociation for aggregates of **2** seem to be significantly faster. In this instance, the emission spectrum (***c*** in Fig. S1), recorded immediately after dilution, reveals already an intense fluorescence, which remains constant for several hours.

In order to elucidate the morphology associated with supramolecular arrays of **1** and **2**, we have analyzed both compounds by environmental scanning electron microscopy (ESEM). Specifically, we have deposited droplets of aqueous solutions of either **1** or **2** on highly-oriented pyrolytic graphite and imaged the sub-

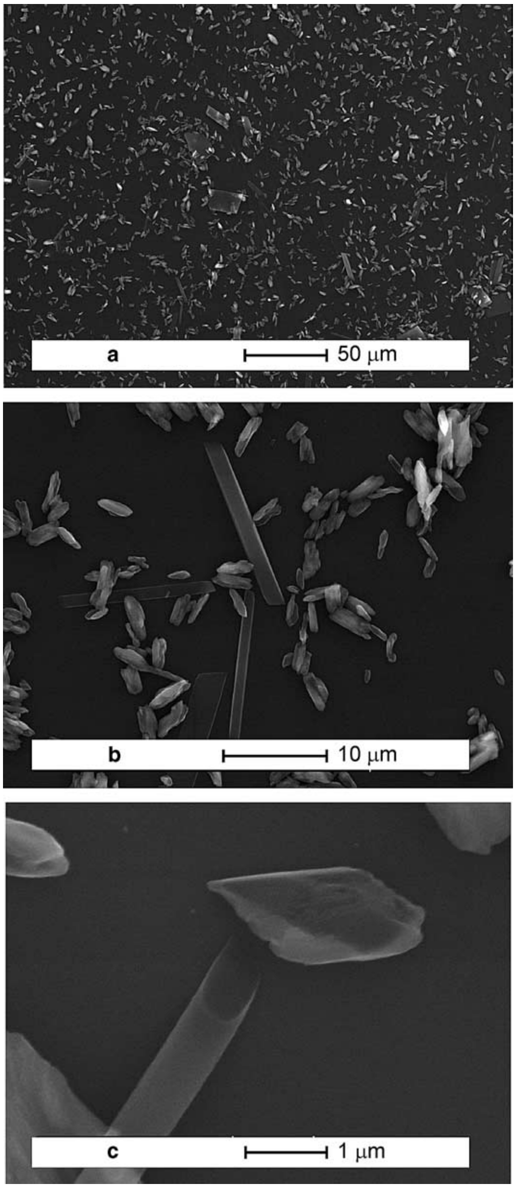


Figure 3. Environmental scanning electron microscopy images (20.0 kV, 0.8 mBar) at increasing magnification (***a–c***) of **2** deposited on highly-oriented pyrolytic graphite.

strates after incubation at 30 °C for 12 h. In the case of **1**, cylindrical microstructures (***a*** and ***b*** in Fig. S2) with dimensions of ca. 2×10 μm are clearly evident in the resulting ESEM images. In the case of **2**, the ESEM images reveal two distinct morphologies (***a–c*** in Fig. 3). In addition to large numbers of irregular aggregates (ca. 1×4 μm), cylindrical features up to 17 μm long and 2 μm wide can be clearly observed.

Similar bolaamphiphiles incorporating carboxylic acids at the ends of aliphatic, rather than aromatic, spacers were also found to aggregate into cylindrical structures.[2a,3a,3d,6d] Infrared spectra of the resulting supramolecular arrays suggested the presence of carboxylate and carboxylic acid groups and the existence of $–CO_2^- \cdots HO_2C–$ hydrogen bonds. A similar analysis of our cylindrical aggregates indicates essentially the same behaviour. Indeed, the infrared spectrum of dried aggregates of **1** (***a*** in Fig. 4) shows three additional peaks at 1724, 1604 and 1441 cm^{-1}, when compared to that of the model compound **3** (***b***). According to the literature data,[13] the peak at 1724 cm^{-1} corresponds to the C=O stretching vibration of hydrogen-bonded carboxylic acids, while those at 1604 and 1441 cm^{-1} are associated with the asymmetrical and symmetrical O=C–O$^-$ stretching vibrations of carboxylate groups. Thus, it is possible that $–CO_2^- \cdots HO_2C–$ hydrogen bonds also contribute to the aggregation of our compounds.

Presumably, the hydrogen bonding interactions suggested by the infrared spectra are corroborated by hydrophobic contacts between the naphthalene diimide cores of our compounds. Indeed, the X-ray structural analysis of single crystals grown from a dimethylsulfoxide solution of **1** agrees with this interpretation. Specifically, the crystal structure of **1** (Fig. 5 and Fig. S3) shows the molecule to be centrosymmetric with the naphthalene diimide core being essentially flat (coplanar to within ca. 0.088 Å). The terminal carboxylic acids are almost orthogonal (ca. 81°) to the plane of the aromatic core and hydrogen bond to the included solvent molecules with [O···O] 2.538(3) Å, [H···O] 1.66 Å and [O–H···O] 163°. The naphthalene diimide cores of adjacent lattice-translated molecules partially overlay each other (Fig. 6) to produce extended stacks of molecules along the crystallographic *b*-axis direction. The centroid···centroid and mean interplanar separations between the hydrophobic cores of adjacent molecules are ca. 5.10 and 3.41 Å, respectively.

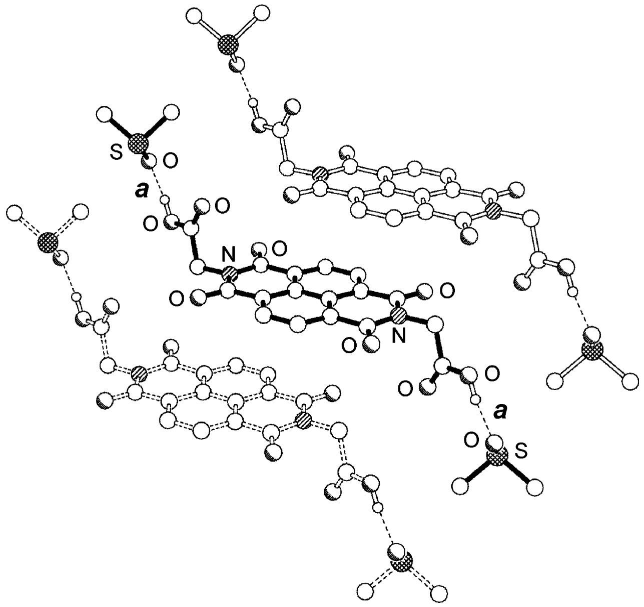
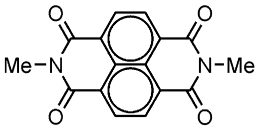


Figure 5. X-ray crystal structure of the C_i-symmetric compound **1** showing the hydrogen bonding (***a***) to the included solvent (dimethylsulfoxide) molecules and the stacking of adjacent naphthalene diimide cores along the crystallographic *b*-axis.



3

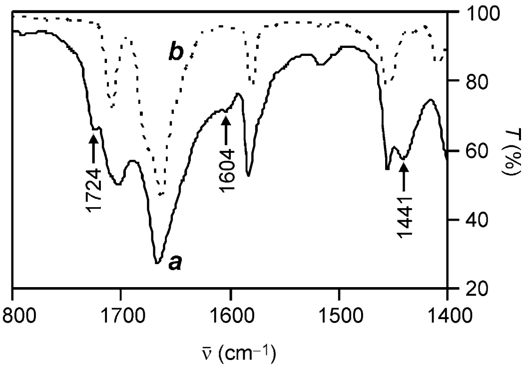


Figure 4. Infrared spectra of the dried aggregates of **1** (***a***) and of a powder of **3** (***b***).

In summary, we have designed two bolaamphiphilic compounds able to self-organize into supramolecular arrays in aqueous solution and, ultimately, produce rod-like microstructures on the surface of solid substrates. Presumably, hydrogen bonds between their carboxylic acid termini and hydrophobic contacts between their naphthalene diimide cores are responsible for the aggregation of these compounds into supramolecular arrays. Furthermore, the chromophoric cores provide the opportunity to probe the supramolecular association

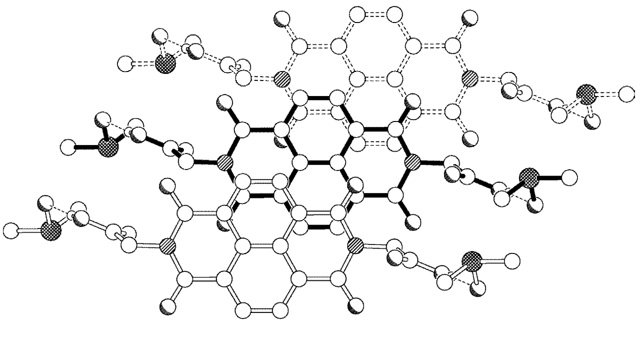


Figure 6. The stacking of adjacent molecules in a single crystal of **1** viewed in parallel projection perpendicular to the plane of the naphthalene diimide cores.

of these compounds in solution with simple absorption and emission spectroscopic measurements. However, the mechanism of formation of the resulting assemblies and the relative orientation of the molecular building blocks within them remain unclear and will require further investigation.

Acknowledgements

We thank the National Institute of Environmental Health Sciences (ES-05705), the National Science Foundation (CAREER Award CHE-0237578) and the University of Miami for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.06.086. Experimental procedures, absorption and emission spectra of **2**, environmental scanning electron microscopy images of **1**, ORTEP representation of the crystal structure of **1**.

References and notes

1. Voet, D.; Voet, J. G. *Biochemistry*; Wiley: New York, 1995.
2. (a) Shimizu, T. *Macromol. Rapid Commun.* **2002**, *23*, 311–331; (b) Estroff, L. A.; Hamilton, A. D. *Chem. Rev.* **2004**, *104*, 1201–1217; (c) Fuhrhop, J.-H.; Wang, T. *Chem. Rev.* **2004**, *104*, 2901–2937.
3. (a) Shimizu, T.; Kogiso, M.; Masuda, M. *Nature* **1996**, *383*, 487–488; (b) Kogiso, M.; Hanada, T.; Yase, K.; Shimizu, T. *Chem. Commun.* **1998**, 1791–1792; (c) Shimizu, T.; Kogiso, M.; Masuda, M. *J. Am. Chem. Soc.* **1997**, *119*, 6209–6210; (d) Kogiso, M.; Ohnishi, S.; Yase, K.; Masuda, M.; Shimizu, T. *Langmuir* **1998**, *14*, 4978–4986; (e) Matsuzawa, Y.; Kogiso, M.; Matsumoto, M.; Shimizu, T.; Shimada, K.; Itakura, M.; Kinugasa, S. *J. Mater. Chem.* **2004**, *14*, 3532–3539.
4. (a) Jokic, M.; Makarevic, J.; Zinic, M. *Chem. Commun.* **1995**, 1723–1724; (b) Makarevic, J.; Jokic, M.; Peric, B.; Tomisic, V.; Kojic-Prodic, B.; Zinic, M. *Chem. Eur. J.* **2001**, *7*, 3328–3341; (c) Frkanec, L.; Jokic, M.; Makarevic, J.; Wolsperger, K.; Zinic, M. *J. Am. Chem. Soc.* **2002**, *124*, 9716–9717.
5. Claussen, R. C.; Rabatic, B. M.; Stupp, S. I. *J. Am. Chem. Soc.* **2003**, *125*, 12680–12681.
6. (a) Shimizu, T.; Masuda, M. *J. Am. Chem. Soc.* **1997**, *119*, 2812–2818; (b) Nakazawa, I.; Masuda, M.; Okada, Y.; Hanada, T.; Yase, K.; Asai, M.; Shimizu, T. *Langmuir* **1999**, *15*, 4757–4764; (c) Nakazawa, I.; Suda, S.; Masuda, M.; Asai, T.; Shimizu, T. *Chem. Commun.* **2000**, 881–882; (d) Masuda, M.; Shimizu, T. *Langmuir* **2004**, *20*, 5969–5977.
7. (a) Newkome, G. R.; Baker, G. R.; Saunders, M. J.; Russo, P. S.; Gupta, V. K.; Yao, Z. Q.; Miller, J. E.; Boullion, K. *J. Chem. Soc., Chem. Commun.* **1986**, 752–753; (b) Newkome, G. R.; Baker, G. R.; Arai, S.; Saunders, M. J.; Russo, P. S.; Theriot, K. J.; Moorefield, C. N.; Rogers, L. E.; Miller, J. E.; Lieux, T. R.; Murray, M. E.; Phillips, B.; Pascal, L. *J. Am. Chem. Soc.* **1990**, *112*, 8458–8465; (c) Newkome, G. R.; Moorefield, C. N.; Baker, G. R.; Behera, R. K.; Escamilla, G. H.; Saunders, M. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 917–919; (d) Newkome, G. R.; Lin, X. F.; Yaxiong, C.; Escamilla, G. H. *J. Org. Chem.* **1993**, *58*, 3123–3129; (e) Escamilla, G. H.; Newkome, G. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1937–1940; (f) Yu, H. K.; Russo, P. S.; Younger, L.; Henk, W. G.; Hua, D. W.; Newkome, G. R.; Baker, G. *J. Polym. Sci. B* **1997**, *35*, 2787–2793.
8. (a) Shimizu, T.; Iwaura, R.; Masuda, M.; Hanada, T.; Yase, K. *J. Am. Chem. Soc.* **2001**, *14*, 5947–5955; (b) Iwaura, R.; Yoshida, K.; Masuda, M.; Yase, K.; Shimizu, T. *Chem. Mater.* **2002**, *14*, 3047–3053; (c) Iwaura, R.; Yoshida, K.; Masuda, M.; Ohnishi-Kameyama, M.; Yoshida, M.; Shimizu, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 1009–1012.
9. Wang, X.; Shen, Y.; Pan, Y.; Liang, Y. *Langmuir* **2001**, *17*, 3162–3167.
10. (a) Kobayashi, H.; Koumoto, K.; Jung, J. H.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1930–1936; (b) Kobayashi, H.; Friggeri, A.; Koumoto, K.; Amaike, M.; Shinkai, S.; Reinhoudt, D. N. *Org. Lett.* **2002**, *4*, 1423–1426.
11. Eastoe, J.; Sánchez-Dominguez, M.; Wyatt, P.; Heenan, R. K. *Chem. Commun.* **2004**, 2608–2609.
12. Abraham, B.; McMasters, S.; Mullan, M. A.; Kelly, L. A. *J. Am. Chem. Soc.* **2004**, *126*, 4293–4300.
13. Ptretsch, E.; Clerc, T.; Seible, J.; Simon, W. *Tables of Spectral Data for Structure Determination of Organic Compounds*; Springer: Berlin, 1989.