The Consequences of Chirality in Crowded Arenes—Macromolecular Helicity, Hierarchical Ordering, and Directed Assembly**

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Complex three-dimensional superstructures with useful properties[1] can be created easily by reversibly assembling functionalized small molecules through hydrogen bonding and π overlap.[2] Examples are **1a** and **1b** (Figure 1a), which self-assemble through head-to-tail amide hydrogen bonds into arrays of stacked columns (Figure 1b, c).[3] In these molecules, the dodecyl ether substituents provide a liquidlike environment, while at the same time they force the amide groups out

1a, R = GlyOtBu; **1b**, R = C₂H₄Ph
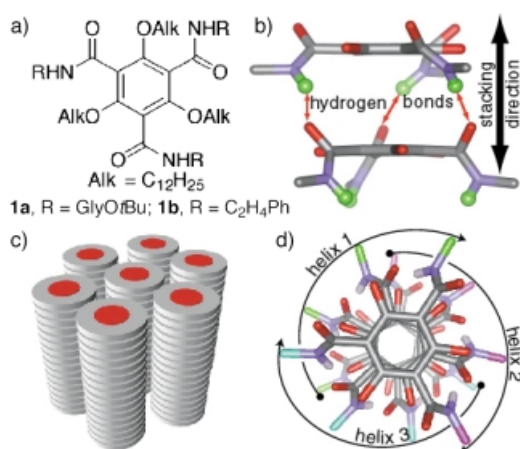
Figure 1. a) Crowded arenes; b) energy-minimized[18] dimer displaying three intermolecular hydrogen bonds; c) hexagonal arrays; d) model of a tetramer showing three helices of hydrogen bonds surrounding the exterior of the column (methyl groups on the ether oxygen atoms were included in the models and removed to clarify the view).

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of the plane of the central aromatic ring. As a consequence, the amide groups are oriented so to form intermolecular hydrogen bonds and therefore stacked structures.[4, 5] Due to this mode of stacking the columns should have a macroscopic dipole moment parallel to the stacking direction (Figure 1b).[6] The study presented here details the macromolecular consequences of synthesizing molecules that are both chiral and liquid crystalline. Neat samples of these mesogens self-assemble into two-dimensional hexagonal arrays that can be directed with electric fields. In dilute solution circular dichroic (CD) spectroscopy shows that the molecules self-assemble into helical stacks. At higher concentrations, these stacks self-organize further into superhelical arrays characteristic of twisted nematic liquid crystals.

For our study we synthesized enantiopure **3a–h** in yields of 47–78% by combining the versatile tris-acylchloride **2**, which can be made on a multigram scale from phloroglucinol,[3] with optically active amines[7] (Scheme 1). The calorimetric values
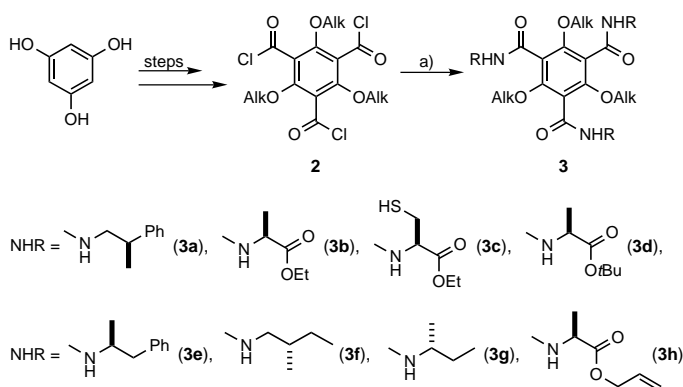
Scheme 1. a) RNH₂, Et₃N, CH₂Cl₂, 47–78%. Alk = C₁₂H₂₅.[8]

(DSC) for **3a–h**[8] vary over a broad range, and many samples exhibit rich polymorphism.[9] One compound, **3a**, emerged as unique from a screening with polarized-light microscopy because it forms a mesophase (191 to 233 °C) that is self-healing and birefringent (Figure 2a).

It is the fluidity that distinguishes the mesophase of **3a** from all of the others. The synchrotron X-ray diffraction[10] pattern from **3a** in a Lindemann capillary tube (Figure 2b) shows an intense, low-angle peak ($d = 18.8$ Å) that is diagnostic of columnar assemblies[11] and two higher-order reflections that allow the lattice to be indexed as two-dimensional hexagonal. In its wide-angle region, the diffractogram shows only a broad reflection ($d \approx 4.8$ Å) that in columnar liquid crystals has been attributed to the packing of fluid side chains.[11] These values correlate well with the lattice parameters previously measured for the columnar, hexagonally ordered achiral **1b**.[3]

Thin samples of **3a**, between ITO-coated glass slides spaced by 5 μm, show uniform birefringent domains that are uniaxial and negatively birefringent (Figure 3a).[12] The implication is that the long axes of the columns are parallel to the surface (the planar alignment).[13] When 30 V is applied between the two electrodes while the material is again cooled into its mesophase, the films are optically isotropic. After removing of the polarizer micron-sized polygons are visible, each having
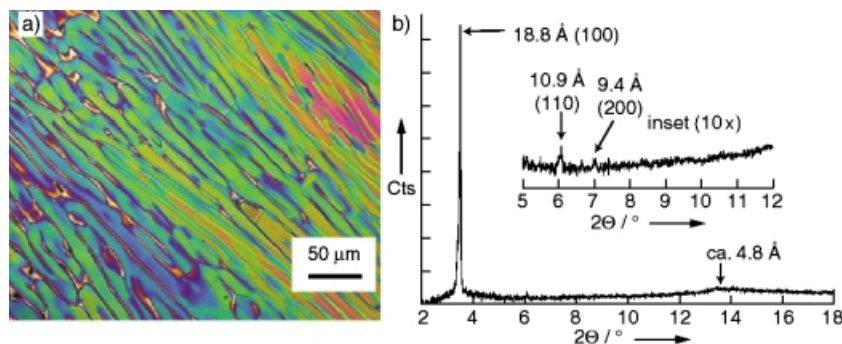
Figure 2. a) View between crossed polarizers at 210 °C as **3a** was cooled from the isotropic liquid. b) Synchrotron X-ray diffraction of **3a** at 220 °C as it was cooled from the isotropic liquid.
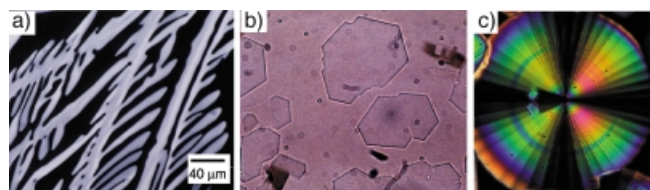

Figure 3. Light micrographs of samples of **3a** cooled to 200 °C from the isotropic liquid: a) optically active, between ITO electrodes separated by 5 μm, 0 V applied; b) optically active, between ITO electrodes separated by 5 μm, 30 V applied; c) racemic **3a** yielding spherulitic crystalline domains.

120° angles at their corners (Figure 3 b), reflecting, in magnified form, the underlying hexagonal lattice symmetry.[14] The implication is that the self-assembly into columns is directed perpendicular to the electrode surface by the applied electric field. When the film is again heated until it is an isotropic liquid and then cooled in the absence of an electric field, the planar alignment returns. Traditionally, discotics are highly viscous and they must be diluted until they are lyotropic nematics to be switched between planar and homeotropic alignments.[15] What is unique about **3a** is that the entire two-dimensional lattice is directed by the electric field and is regularly arrayed over μm-sized length scales (Figure 3 b). Molecular models indicate that polarity in the columns of **3a** results from the head-to-tail orientation of the amide side chains, as shown in Figure 1 d, creating a macroscopic dipole moment parallel to the column axis.

Both racemic (±)-**3a**[16] and a sample of **3a** that is a mixture of diastereomers [(dia)-**3a**][17] were prepared to test whether the chirality is involved in the liquid crystallinity and polarity of **3a**. The clearing points for pure **3a**, (±)-**3a**, and (dia)-**3a** were all within a few degrees indicating that the differences in their assemblies must be slight. The textures displayed by samples of (±)-**3a** (Figure 3 c) and (dia)-**3a** as they are cooled from their isotropic states are those of spherulitic, crystalline materials. This is the same texture seen previously in the hexagonally ordered plastic crystals of **1b**, whose molecules lack the angular methyl groups.[3] Neither (±)-**3a** nor (dia)-**3a** nor **1b** show an electrical response like that seen for optically active **3a**. The spherulitic textures persist even when up to 100 V is applied between the electrodes. Models, like the one in Figure 1 d,[18] constructed with the optically active side chains of **3a**, show that in the stacked molecules the phenyl groups in the side chains touch the methyl groups of their

nearest neighbors. These interactions provide a mechanism for the optically active side chains to stabilize the helicity of the columns. In the racemic or diastereomeric material, these contacts are absent.

CD spectroscopy[19] was used to analyze the stacks because it has proven to be a sensitive reporter of helicity, through the coupling of transition dipoles, in polypeptides,[20] other polymers,[22–26] and discotic liquid crystals.[6e, 21] Solutions of **3a** in hexane were not homogeneous but could be made so by dilution with ca. 15% CH_2Cl_2. At these concentrations, the CD transitions of **3a** show an exciton coupling between degenerate chromophores (a split CD, Figure 4 b) indicative of helical order. As more CH_2Cl_2 is added (30%), the aggregates dissociate and the transition dipoles no longer couple. Thus, only when the solvent is hydrocarbonlike do the molecules self-assemble through hydrogen bonds with their side chains close enough to interact with each other. Evidence that it is the contact between the methyl and phenyl groups that stabilizes the helices comes from studies with optically active **3f**, whose chirality arises only from the difference between a methyl and an ethyl group. It has no phenyl group in the side chains and its mesophase, shown in Figure 6 a, looks like that of achiral **1a**.[3]
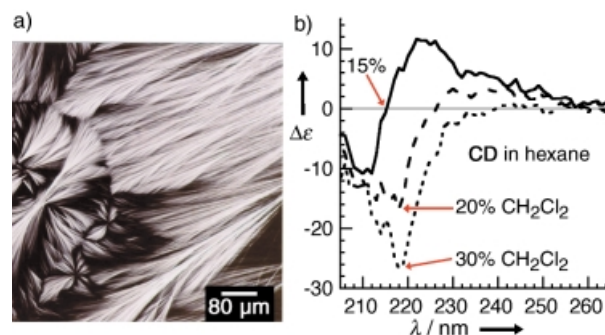

Figure 4. a) Polarized-light micrograph of fibrous **3a** grown from a hot dodecane solution; b) CD spectra of **3a** in hexane (7.5×10^{-4} M, path length = 100 μm).

If the aggregates of **3a** are helical and have a significant persistence length, they could display the common assembly motif of helically wound polymers that pack next to one another with defined twist angles.[22–26] As this twist is propagated through the assembly, it gives rise to a superhelical structure (Figure 5 c) like that of a twisted nematic liquid crystal. This type of liquid crystalline phase is uncommon in classic discotics possibly due to the low association in the stacking direction. Unfortunately, concentrated solutions of **3a** could not be tested for such a phase behavior because **3a** is insufficiently soluble in hydrocarbon solvents. (It forms the fibrous aggregates shown in Figure 4 a.) However, **3a** is soluble up to 50 wt % in dodecane when it is mixed with **1a**! We presume this is because **1a** frustrates the ability of **3a** to crystallize from hydrocarbon solvent into fibers.

The CD spectra of dilute solutions of the **1a/3a** mixture are split, just like the spectra of **3a** discussed above. At high concentrations, the samples visibly reflect green light. Their CD spectra, an example of which is in Figure 5d, show intense
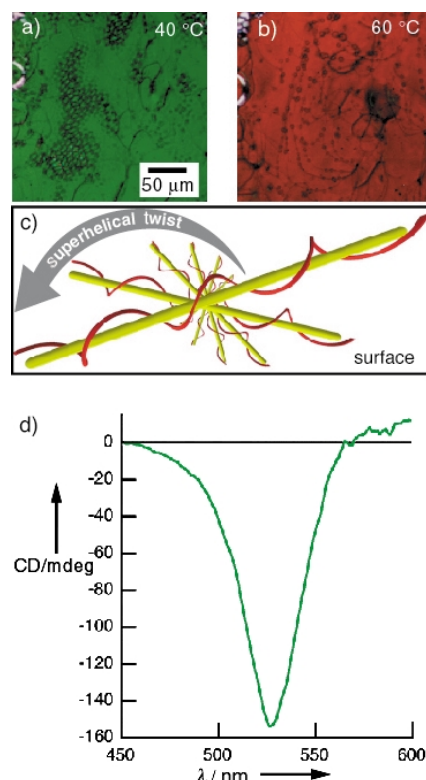

Figure 5. Studies on **3a/1a** (25% each by weight) solutions in dodecane. a) Polarized-light micrograph at 40 °C, b) at 60 °C; c) model of the super-helical arrangement of columns; d) CD spectrum at room temperature.

transitions at 525 nm,[27] attributed to the selective reflection of circularly polarized light by the twisted nematic phase.[28] The superhelical pitch expands when the temperature is raised, so the reflection is green at room temperature (Figure 5a) and red at 60 °C (Figure 5b). Concentrated **1a/3d** mixtures in dodecane diplay a "fingerprint" texture also characteristic of twisted nematic liquid crystals.[29] Twisted nematic phases are rare for self-assembled columnar structures,[21a] and the reason for their being seen in this study is that the hydrogen bonds working in concert with the chiral side chains enforce a regular helicity and a high association constant in the stacking direction. In essence, the aggregates in solution act as noncovalent polymers.[28]

It is remarkable that just moving the methyl group in the amide side chain from the β position in **3a** to the α position in **3e** changes the morphologies drastically as shown in Figures 2a and 6b. In fact, with the exception of the extremely hindered **3d**, all the molecules with chiral centers adjacent to the nitrogen atom (**3b,c,e,g,h**) lead to μm-sized birefringent fibers as the materials are cooled from their isotropic liquid states. Like the fibers from other columnar systems,[13] these too are uniaxial and negatively birefringent.[12] X-ray diffraction shows these fibrous samples to consist of a two-dimensional hexagonal lattice of columns. Unlike the diffractogram
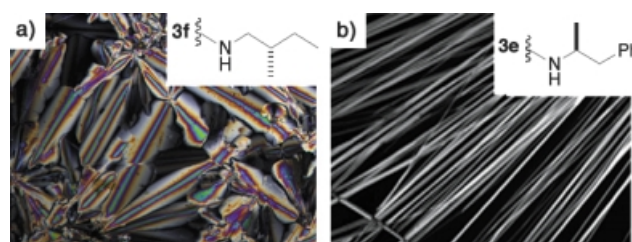

Figure 6. View between crossed polarizers as the samples were cooled from the isotropic liquid. a) **3f** at 197 °C; b) **3e** at 246 °C.

of the liquid crystalline phase of **3a**, the ones from the fibers of **3b,c, e,g,h** reveal larger lattice spacings and contain numerous, sharp higher-order reflections indicative of a crystalline phase with the columns running parallel to the fiber axis.[13c, 30] These results show how seemingly minor variations in molecular structure can have drastic impacts on the resulting morphology and phase behavior.

In summary, we have shown that chiral side chains can be easily installed into the crowded nucleus of **1** and that they control the hierarchy of ordering in the stacks. First, the chiral centers in the side chains organize the columns into helices. These chiral columns further stack in concentrated solutions to create superhelical arrangements that reflect circularly polarized light at resonant wavelengths. In the neat samples the materials self-organize into hexagonally arranged fibers or liquid crystalline phases depending on where the chiral center is positioned. Some of these chiral phases are responsive to electric fields and their assembly can be directed from electrode surfaces. It is possible that these nanostructured columns may act as ferroelectric, piezoelectric, and other types of responsive materials.

[1] a) G. M. Whitesides, J. P. Mathias, C. T. Seto, *Science* **1991**, *254*, 1312 – 1319; b) J.-M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, **1995**; c) D. Philp, J. F. Stoddart, *Angew. Chem.* **1996**, *108*, 1242 – 1286; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1155 – 1196; d) M. Muthukumar, C. K. Ober, E. L. Thomas, *Science* **1997**, *277*, 1225 – 1232.

[2] Hydrogen bonds in liquid crystals: a) T. Kato in *Handbook of Liquid Crystals, Vol. 2b* (Eds.: D. Demus, J. W. Goodby, G. W. Gray, H. W. Spiess, V. Vill), Wiley-VCH, Weinheim, **1998**, pp. 969 – 979; b) A. H. Simmons, C. A. Michal, L. W. Jelinski, *Science* **1996**, *271*, 84 – 87; c) C. M. Paleos, D. Tsiourvas, *Angew. Chem.* **1995**, *107*, 1839 – 1855; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1696 – 1711; d) V. V. Tsukruk, *Prog. Polym. Sci.* **1997**, *22*, 247 – 311; e) C. Fouquey, J.-M. Lehn, A.-M. Levelut, *Adv. Mater.* **1990**, *2*, 254 – 257; f) T. Gulik-Krzywicki, C. Fouquey, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 163 – 167; g) R. K. Castellano, C. Nuckolls, S. H. Eichhorn, M. R. Wood, A. J. Lovinger, J. Rebek, Jr., *Angew. Chem.* **1999**, *111*, 2764 – 2768; *Angew. Chem. Int. Ed.* **1999**, *38*, 2603 – 2606.

[3] M. L. Bushey, A. Hwang, P. W. Stephens, C. Nuckolls, *J. Am. Chem. Soc.* **2001**, *123*, 8157 – 8158.

[4] Leading references on discotic liquid crystals: a) D. Guillon, *Struct. Bonding* **1999**, *95*, 41 – 82; b) S. Chandrasekhar, G. S. Ranganath, *Rep. Prog. Phys.* **1990**, *53*, 57 – 84.

[5] Amides used to organize discotic liquid crystals: a) C. M. Paleos, D. Tsiourvas, *Angew. Chem.* **1995**, *107*, 1839 – 1855; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1696 – 1711, and references therein; b) Y. Matsunaga, N. Miyajima, Y. Nakayasu, S. Sakai, M. Yonenaga, *Bull.*

Chem. Soc. Jpn. **1988**, *61*, 207–210; c) A. R. A. Palmans, J. A. J. M. Vekemans, H. Fischer, R. A. Hikmet, E. W. Meijer, *Chem. Eur. J.* **1997**, *3*, 300–307; d) M.-J. Brienne, J. Gabard, J.-M. Lehn, I. Stibor, *J. Chem. Soc. Chem. Commun.* **1989**, 1868; e) D. Goldmann, R. Dietel, D. Janietz, C. Schmidt, J. H. Wendorff, *Liq. Cryst.* **1998**, *24*, 407–411; f) G. Ungar, D. Abramic, V. Percec, J. A. Heck, *Liq. Cryst.* **1996**, *21*, 73–86; g) V. Percec, C.-H. Ahn, T. K. Bera, G. Ungar, D. J. P. Yeardley, *Chem. Eur. J.* **1999**, *5*, 1070–1083; h) L. Brunsveld, H. Zhang, M. Glasbeek, J. A. J. M. Vekemans, E. W. Meijer, *J. Am. Chem. Soc.* **2000**, *122*, 6175–6182, and references therein; i) J. Malthête, A. M. Levelut, L. Liebert, *Adv. Mater.* **1992**, *4*, 37–41; j) D. Pucci, M. Veber, J. Malthête, *Liq. Cryst.* **1996**, *21*, 153–155.

[6] Similar to the dipole moment that is generated in the following systems: a) vanadyl liquid crystals: D. Kilian, D. Knawby, M. A. Athanassopoulou, S. T. Trzaska, T. M. Swager, S. Wrobel, W. Haase, *Liq. Cryst.* **2000**, *27*, 509–521; b) pyramidic liquid crystals: H. Zimmermann, R. Poupko, Z. Luz, J. Billard, *Z. Naturforsch. A* **1985**, *40*, 149–160; c) J. Malthête, A. Collet, *J. Am. Chem. Soc.* **1987**, *109*, 7544–7545; d) helicene liquid crystals: C. Nuckolls, T. J. Katz, *J. Am. Chem. Soc.* **1998**, *120*, 9541–9544.

[7] All of the amines were commercially available in nonracemic form with the exception of the one that yields **3d**. It was synthesized by a known procedure: D. A. Quagliato, P. M. Andrae, E. M. Matelan, *J. Org. Chem.* **2000**, *65*, 5037–5042.

[8] Detailed synthetic procedures and differential scanning calorimetry (DSC) data are contained in the Supporting Information.

[9] Their transition enthalpies vary between 1 and 40 kJ mol^{-1}. The low-temperature phases in samples that display several phase transitions are difficult to characterize because their powder X-ray diffracto-grams are extremely complex and their morphology is that of small grains.

[10] Samples were loaded into 1 mm Lindemann capillary tubes that were rotated during data acquisition to eliminate any artifacts due to preferential alignment.

[11] a) A. M. Levelut, *J. Chim. Phys. Phys.-Chim. Biol.* **1983**, *80*, 149–161; b) the citations in ref. [4].

[12] N. H. Hartshorne, A. Stuart, *Crystals and the Polarising Light Microscope*, 3rd ed., Edward Arnold Ltd., London, **1960**, p. 290 ff.

[13] Negatively birefringent discotics and discotic fibers: a) C. Vauchier, A. Zann, P. Le Barny, J. C. Dubois, J. Billard, *Mol. Cryst. Liq. Cryst.* **1981**, *66*, 423–433; b) A. J. Lovinger, C. Nuckolls, T. J. Katz, *J. Am. Chem. Soc.* **1998**, *120*, 264–268.

[14] Hexagonal domains are an indicator of homeotropic alignment in discotics: a) C. Destrade, P. Foucher, H. Gasparoux, H. T. Nguyen, A. M. Levelut, J. Malthête, *Mol. Cryst. Liq. Cryst.* **1984**, *106*, 121–146; b) J. Billard, J. C. Dubois, H. T. Nguyen, A. Zann, *Nouv. J. Chim.* **1978**, *2*, 535–540; c) Y. Bouligand, *J. Phys.* **1980**, *41*, 1307–1315; d) S. D. Hudson, H. T. Jung, V. Percec, W.-D. Cho, G. Johansson, G. Ungar, V. S. K. Balagurusamy, *Science* **1997**, *278*, 449–452; e) V. Percec, G. Johansson, G. Ungar, J. Zhou, *J. Am. Chem. Soc.* **1996**, *118*, 9855–9866.

[15] a) C. Nuckolls, R. Shao, W.-G. Jang, N. A. Clark, D. M. Walba, T. J. Katz, *Chem. Mater.* **2002**, *14*, 773–776; b) A. R. A. Palmans, J. A. J. M. Vekemans, R. A. Hikmet, H. Fischer, E. W. Meijer, *Adv. Mater.* **1998**, *10*, 873; c) N. Usol'tseva, G. Hauck, H. D. Koswig, K. Praefcke, B. Heinrich, *Liq. Cryst.* **1996**, *20*, 731; d) D. Krüerkke, P. Rudquist, S. T. Lagerwall, H. Sawade, G. Heppke, *Ferroelectrics* **2000**, *243*, 207.

[16] Racemic mixtures were made by mixing equimolar amounts of the optically pure enantiomers.

[17] A mixture of diastereomers was synthesized by using a racemic mixture of a chiral amine to react with the tris-acylchloride **2**.

[18] Molecular modeling performed with MacroModel Version 7.0 (Amber*): F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440–467.

[19] N. Harada, K. Nakanishi, *Circular Dichroic Spectroscopy – Exciton Coupling in Organic Stereochemistry*, University Science Books, Mill Valley, CA, **1983**.

[20] C. Branden, J. Tooze, *Introduction to Protein Structure*, 2nd ed, Garland Publishing, New York, NY, **1998**.

[21] Similar to the enhancements seen with other chiral columnar aggregates: a) G. Gottarelli, E. Mezzina, G. P. Spada, F. Carsughi, G. Di Nicola, P. Mariani, A. Sabatucci, S. Bonazzi, *Helv. Chim. Acta* **1996**, *79*, 220, and references therein; b) A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga, E. W. Meijer, *Angew. Chem.* **1997**, *109*, 2763–2765; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2648; c) S. T. Trzaska, H.-F. Hsu, T. M. Swager, *J. Am. Chem. Soc.* **1999**, *121*, 4518–4519; d) C. F. van Nostrum, A. W. Bosman, G. H. Gelinck, P. G. Schouten, J. M. Warman, A. P. M. Kentgens, M. A. C. Devillers, A. Meijerink, S. J. Picken, U. Sohling, A.-J. Schouten, R. J. M. Nolte, *Chem. Eur. J.* **1995**, *1*, 171–182; e) H. Engelkamp, C. F. van Nostrum, R. J. M. Nolte, S. J. Picken, *Chem. Commun.* **1998**, *9*, 979–980.

[22] A. A. Kornyshev, S. Leikin, *Phys. Rev. E* **2000**, *62*, 2576–2596, and references therein.

[23] DNA and nucleic acid derivatives: a) F. Livolant, A. M. Levelut, J. Doucet, J. P. Benoit, *Nature* **1989**, *339*, 724; b) K. Merchant, R. L. Rill, *Biophys. J.* **1997**, *73*, 3154–3163; c) R. L. Rill, F. Livolant, H. C. Aldrich, M. W. Davidson, *Chromosoma* **1989**, *98*, 280–286; d) G. Gottarelli, G. Proni, G. P. Spada, S. Bonazzi, A. Garbesi, F. Ciuchi, P. Mariani, *Biopolymers* **1997**, *42*, 561–574; e) G. Proni, G. Gottarelli, P. Mariani, G. P. Spada, *Chem. Eur. J.* **2000**, *6*, 3249–3253.

[24] In polypeptides: a) D. B. DuPré, E. T. Samulski in *Liquid Crystals — The Fourth State of Matter* (Ed.: F. Saeva), Dekker, New York, NY, **1979**; b) T. Hashimoto, S. Ebisu, N. Inaba, H. Kawai, *Polym. J.* **1981**, *13*, 701–713.

[25] a) X. M. Dong, D. G. Gray, *Langmuir* **1997**, *13*, 3029–3034; b) T. Sato, J. Nakamura, A. Teramoto, M. M. Green, *Macromolecules* **1998**, *31*, 1398–1405.

[26] T. Sato, Y. Sato, Y. Umemura, A. Teramoto, Y. Nagamura, J. Wagner, D. Weng, Y. Okamoto, K. Hatada, M. M. Green, *Macromolecules* **1993**, *26*, 4551–4559.

[27] Although the CD spectra of all the rotations were very similar, the spectrum displayed in Figure 5d is an average of 24 rotations each through 15° to eliminate any artifacts from linear dichroism, a procedure similar to that of experiments with linear polymers and aggregates: a) A. Schoenhofer, H. G. Kuball, *Chem. Phys.* **1987**, *115*, 159–167; b) B. Norden, *Acta Chem. Scand.* **1972**, *26*, 1763–1776; c) M. J. B. Tunis-Schneider, M. F. Maestre, *J. Mol. Biol.* **1970**, *52*, 521–541; d) D. G. Cornell, *Colloid Interface Sci.* **1979**, *70*, 167–180; e) C. Nuckolls, T. J. Katz, T. Verbiest, S. Van Elshocht, H.-G. Kuball, S. Kiesewalter, A. J. Lovinger, A. Persoons, *J. Am. Chem. Soc.* **1998**, *120*, 8656–8660.

[28] J. S. Moore, *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 108–116.

[29] For selective reflection and fingerprint textures from twisted nematics see: H. Coles in *Handbook of Liquid Crystals*, *Vol. 2b*, (Eds.: D. Demus, J. W. Goodby, G. W. Gray, H. W. Spiess, V. Vill), Wiley-VCH, Weinheim, **1998**, pp. 335–409.

[30] Similar to the orientation described in: a) M. R. Ghadiri, J. R. Granja, R. A. Milligan, D. E. McRee, N. Khazanovich, *Nature* **1993**, *366*, 324–327; b) H. Engelkamp, S. Middelbeek, R. J. M. Nolte, *Science* **1999**, *284*, 785–788; c) I. S. Choi, X. Li, E. E. Simanek, R. Akaba, G. M. Whitesides, *Chem. Mater.* **1999**, *11*, 684–690.