Angewandte Chemie International Edition

DOI: 10.1002/anie.201308462

Carbon Materials

Helical Carbon and Graphite Films Prepared from Helical Poly(3,4-ethylenedioxythiophene) Films Synthesized by Electrochemical Polymerization in Chiral Nematic Liquid Crystals**

*Satoshi Matsushita, Bairu Yan, Shinsuke Yamamoto, Yong Soo Jeong, and Kazuo Akagi**

Abstract: *Helical carbon and graphite films from helical poly(3,4-ethylenedioxythiophene) (H-PEDOT) films synthesized through electrochemical polymerization in a chiral nematic liquid-crystal (N*-LC) field are prepared. The microscope investigations showed that the H-PEDOT film synthesized in the N*-LC has large domains of one-handed spiral morphology consisting of fibril bundles. The H-PEDOT films exhibited distinct Cotton effects in circular dichroism spectra. The highly twisted N*-LC with a helical pitch of smaller than 1 μm produced the H-PEDOT film with a highly ordered morphology. The spiral morphologies with left- and right-handed screws were observed for the carbon films prepared from the H-PEDOT films at 800°C and were well correlated with the textures and helical pitches of the N*-LCs. The spiral morphologies of the precursors were also retained even in the graphite films prepared from the helical carbon films at 2600°C.*

Helical carbon and graphite films with tunable helical sense and degree of helicity are potentially applicable materials in carbon-based electronics and nanotechnology because of their electrical conductivity, high chemical and thermal stability, and chirality derived from the helical structure. However, it is intrinsically difficult to fabricate a carbon film with a unique morphology, such as a hierarchical helical structure. Although vapor-phase carbonization can produce newly discovered allotropes of carbon such as fullerenes, carbon nanotubes, and graphenes, there are some limitations in producing carbon films with hierarchical morphology using the carbonization method. In contrast, solid-state carbonization of an organic polymer film with controlled morphology can be regarded as a promising approach for the fabrication of the carbon films with hierarchical morphology if the precursor morphology is preserved during the carbonization, even at high temperature. Recently, chiral nematic (N*) mesoporous carbon films with a high specific surface area that have been prepared from nanocrystalline cellulose-silica composite films serving as carbonization precursors have been reported.[1]

Currently, the development of the “morphology-retaining carbonization method” has demonstrated that iodine-doped helical polyacetylene (H-PA) films are promising precursors to produce helical graphite films with unique spiral morphologies consisting of helical graphite fibers.[2] The H-PA films are synthesized through asymmetric interfacial polymerization in N* liquid-crystal (N*-LC) fields.[3] However, further improvements in efficiency and effectiveness for the preparation of helical graphite films are desired. To this end, the following two possible approaches are considered appropriate for improving the carbonization method. One is 1) to use the electrochemical polymerization for the synthesis of the carbonization precursors which is easier and safer than the interfacial acetylene polymerization and can operate under ambient conditions.[4] The other is 2) to use the helical aromatic π-conjugated polymers as stable precursors instead of the helical aliphatic ones with poor stability. The inherently rigid backbone of the aromatic π-conjugated polymers will suppress thermal degradation and will provide high thermal durability during the carbonization process.

The asymmetric polymerization method using the N*-LC as a reaction field has profound versatility for the synthesis of helical π-conjugated polymers that do not even have chiral substituents on side chains.[5] In particular, the helical poly(3,4-ethylenedioxythiophene) (H-PEDOT) film electrochemically synthesized in N*-LC shows clear spiral morphology with electroactive properties.[6] One of the feasible ways of preparing helical graphite films is to use the helical π-conjugated polymer films with spiral morphology based on both of the above-described two approaches. In this study, we prepared helical carbon and graphite films from the H-PEDOT films as potential carbonization precursors. The H-PEDOT films were synthesized through asymmetric electrochemical polymerization of bis-EDOT in N*-LC containing an electrolyte (Scheme 1). Here we present a new aspect of aromatic π-conjugated polymers by focusing on their availability as precursors in preparing helical carbon and graphite films.

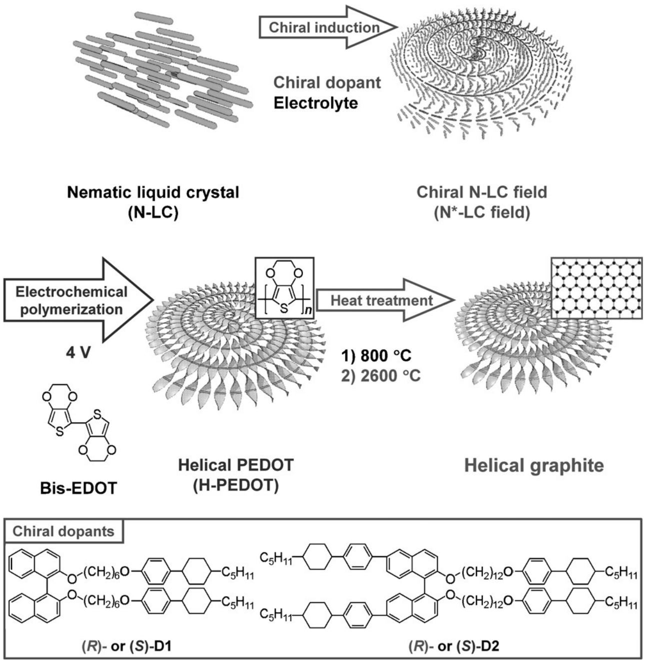
Scheme 1 depicts the molecular structures of the di- and tetra-substituted axially chiral dopants, D1 and D2, respectively. The N*-LC of systems 1–3 were prepared by adding D1

---

[*] Dr. S. Matsushita, B. Yan, S. Yamamoto, Dr. Y. S. Jeong, Prof. K. Akagi
Department of Polymer Chemistry, Kyoto University
Katsura, Kyoto 615-8510 (Japan)
E-mail: akagi@fps.polym.kyoto-u.ac.jp

[**] We would like to thank Dr. A. Kaito and Dr. M. Shimomura (AIST, Japan) for the measurements of Raman spectra, Dr. S. Ohshima and Dr. T. Saito (AIST, Japan) for the use of the graphitizing apparatus. The authors are grateful to Dr. M. Kyotani (University of Tsukuba, Japan) for his helpful cooperation and support. The authors are also grateful to laboratory colleague Mr. C. Tao (Kyoto University, Japan) for his experimental support. This work was supported by the Ministry of Education, Culture, Sports, Science and Technology (Japan) through a grant-in-aid for scientific research (S, grant number 20225007 and A, grant number 13370214), and a grant-in-aid for young scientists (B, grant number 24750219).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201308462.



Scheme 1. Preparation of a helical graphite film using the carbonization of a H-PEDOT film synthesized in an N*-LC field and molecular structures of the chiral dopants.

or D2 into an N-LC, 4-cyano-4′-*n*-pentylbiphenyl (5CB; see the Experimental Section). Figure 1 shows UV/Vis, circular dichroism (CD), and g_{abs} spectra of the oxidized and neutral H-PEDOT films synthesized in N*-LC of system 3 including D2. The as-grown PEDOT film including the perchlorate ion (ClO_4^-) as a dopant species is called the "oxidized PEDOT film" hereafter. The electrochemically produced aromatic π-conjugated polymers are usually obtained in a doped (oxidized) state. The oxidized PEDOT film can be reduced to produce a "neutral PEDOT film" through an electrochemical dedoping process, although the reduction is not completely achieved (for details see the Supporting Information). The neutral H-PEDOT films showed bisignate Cotton effects in the CD spectra, which indicates the formation of a polymer assembly with an interchain helically π-stacked structure.[7] According to the exciton coupling theory,[8] the (*R*)- and (*S*)-PEDOT films have right-handed (*P*-helicity) and left-handed (*M*-helicity) helical senses, respectively. The degree of circular polarization in absorption was evaluated using the dissymmetry factor, g_{abs}. This factor is defined by the equation $g_{abs} = 2(\varepsilon_L - \varepsilon_R)/(\varepsilon_L + \varepsilon_R) = \Delta\varepsilon/\varepsilon$. The H-PEDOT films had values of g_{abs} on the order of 10^{-2} in the absorption region. From these results, the H-PEDOT films are anticipated to yield chiral carbonization precursors bearing interchain one-handed helical π-stacked structures.

Figure 2 shows polarizing optical microscope (POM) and scanning electron microscope (SEM) images of the neutral H-PEDOT films synthesized in N*-LCs of system 3 with a helical pitch of 341 nm (see Table S1 in the Supporting Information). The SEM images show the formation of a large domain of spiral morphology that is composed of a fibrous structure. The screw direction of the spiral is opposite to the helical sense of the N*-LC (Table S2).[9] The H-PEDOT film synthesized using mono-EDOT as a monomer has no fibril morphology but only shows a fingerprint texture.[6a] The use of bis-EDOT with a rigid, rod-like molecular shape and a lower oxidation potential causes a directional polymer growth and the production of polymers with a high conversion rate, resulting in a fibril structure. In fact, the oxidation potential (E_{pa}) of the EDOT dimer (0.9 V) is much lower than that of the EDOT monomer (1.5 V).[10] It is considered that the high planarity of EDOT itself also facilitates positive effects for the formation of the PEDOT fibrils. There are several investigations about the chemical synthesis of π-conjugated polymers with fiber structures such as polyanilines, polypyrroles, and PEDOTs.[11] From the viewpoint of evaluating one-dimensionality in physical, chiroptical, and electromagnetic properties, fiber-structured materials are favorable. The distance between the fibril bundles (150 nm) is very close to the half-helical pitch of the N*-LC (about 170 nm).[12] The distance can be controlled by choosing the chirality and concentration of the chiral

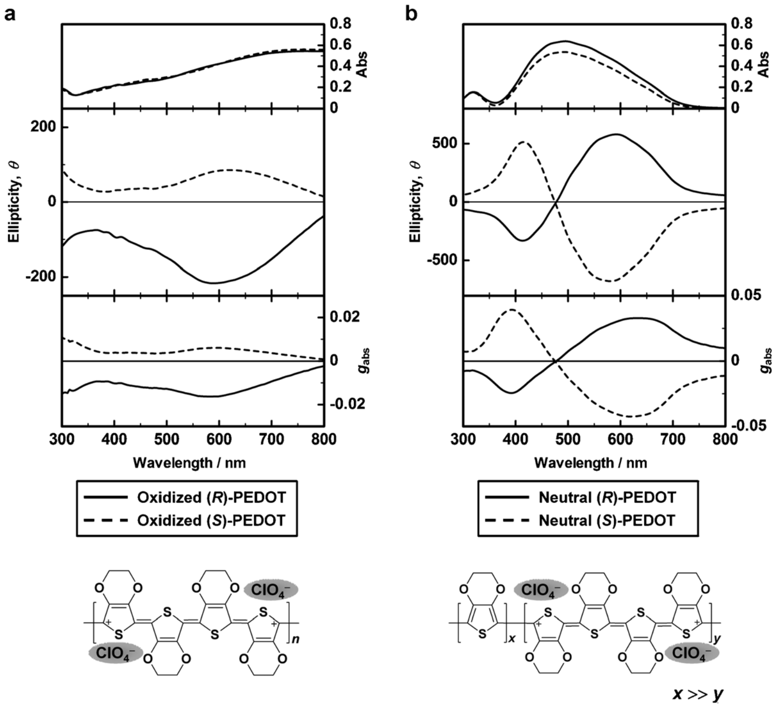


Figure 1. UV/Vis, CD, and g_{abs} spectra of the a) oxidized ("as-polymerized") and b) neutral H-PEDOT films synthesized in N*-LCs of system 3 [polymerization; 5CB:(*R*)- or (*S*)-D2:bis-EDOT:TBAP = 100:1:2:0.2 (mole ratio), ITO glass (anode), ITO glass (cathode), 4 V, 5 minutes, 20 °C] [dedoping; TBAP: 0.05 M, in MeCN, Pt wire (anode), ITO glass (cathode), 4 V, 5 minutes, room temperature]. (*R*)- and (*S*)-PEDOT denote the H-PEDOT films synthesized in N*-LCs including the chiral dopants of (*R*)- and (*S*)-configurations, respectively. UV/Vis spectra of the neutral H-PEDOT films have a λ_{max} of 493–495 nm.

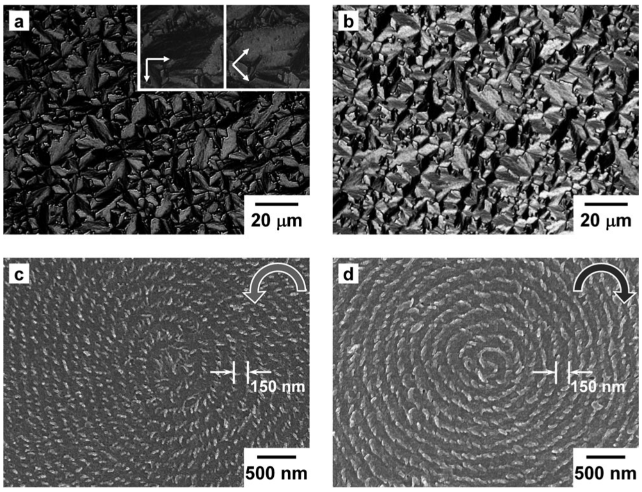


Figure 2. POM images of the neutral H-PEDOT films synthesized in a) (*R*)- and b) (*S*)-N*-LCs of system 3, respectively [5CB:(*R*)- or (*S*)-D2:bis-EDOT:TBAP = 100:1:2:0.2]. Arrows indicate the directions of the polarizer and analyzer. SEM images of c) left- and d) right-handed H-PEDOT films with spiral morphologies synthesized using c) (*R*)- and d) (*S*)-D2, respectively.

dopant. The H-PEDOT films synthesized in N*-LCs of systems 1 and 2 had the distance of 1.5–1.6 μm and 270–280 nm, respectively (Figures S1–S3). The highly twisted H-PEDOT film synthesized in N*-LC including D2 shows an intense CD signal (Figure 1) with crystal-like ordered morphology (Figure 2 a,b, and Figures S4–S6). The chiral dopant of D2 induces highly twisted N*-LC with a helical pitch of 341–621 nm.[13] This is approximately five to nine times shorter than the helical pitch of N*-LC induced by the chiral dopant of D1 (3.1 μm). The addition of a small amount of D2 (0.5–1 mol %) into an N-LC enabled us to prepare a highly twisted N*-LC; the molar concentration of the chiral dopant in systems 2 and 3 is one-half of or equal to that of D1 in system 1 (Table S1). The g_{abs} of the neutral H-PEDOT film synthesized in system 3 was higher than that of the H-PEDOT film synthesized in system 1 (Figure 1 and Figure S7).

The X-ray diffraction (XRD) analyses for the graphite films prepared from the oxidized and neutral PEDOT films at 800 °C and subsequent heating at 2600 °C (abbreviated as oxidized and neutral PEDOT-2600 films) indicated that the former has a higher crystallinity than the latter (Figure 3 a,b and Figure S8).[14] The oxidized PEDOT-2600 film shows a sharp (002) plane of a graphitic crystal at 3.46 Å (25.7° in 2θ). This is attributed to the difference in crystallinity between the neutral and oxidized PEDOT films as carbonization precursors.[15] The closely packed polymer chains stabilized by the doped ClO_4^- ions in the oxidized PEDOT film will crosslink effectively during the heating process. As a result, the graphitized PEDOT film with high crystallinity is prepared from the oxidized PEDOT film. The electrical conductivity of the graphite film is on the order of 10 S cm^{-1}. The Raman spectrum of the carbon film shows a broad band at 1358 cm^{-1} that is attributed to the disordered structure (D-band) and a strong peak at 1589 cm^{-1} corresponding to the graphitic structure of the sp^2 hexagonal carbon network (G-band). The two Raman bands at 1358 and 1589 cm^{-1} become sharp, and at the same time, the former and the latter decreases and increases in intensity, respectively, after the graphitization (Figure 3 c and d). If the oxidized H-PEDOT films are used as carbonization and graphitization precursors, the preparation of helical graphite films with a high crystallinity can be expected. Therefore, the oxidized H-PEDOT films were employed as precursors.

The X-ray photoelectron spectroscopy (XPS) measurement of the PEDOT-800 films was achieved to investigate the quantitative sulfur content and bonding states of sulfur in the carbon film. The XPS survey spectra showed O 1s, C 1s, S 2s, and S 2p peaks. The C 1s peak increased considerably and the O 1s and S 2p peaks decreased in intensity, respectively, after carbonization at 800 °C. The PEDOT-800 films have no Cl 2p peak on the surface that is in agreement with the result of the elemental analysis. Figure 3 e and f shows high-resolution C 1s and S 2p spectra of the oxidized PEDOT-800 film, respec-

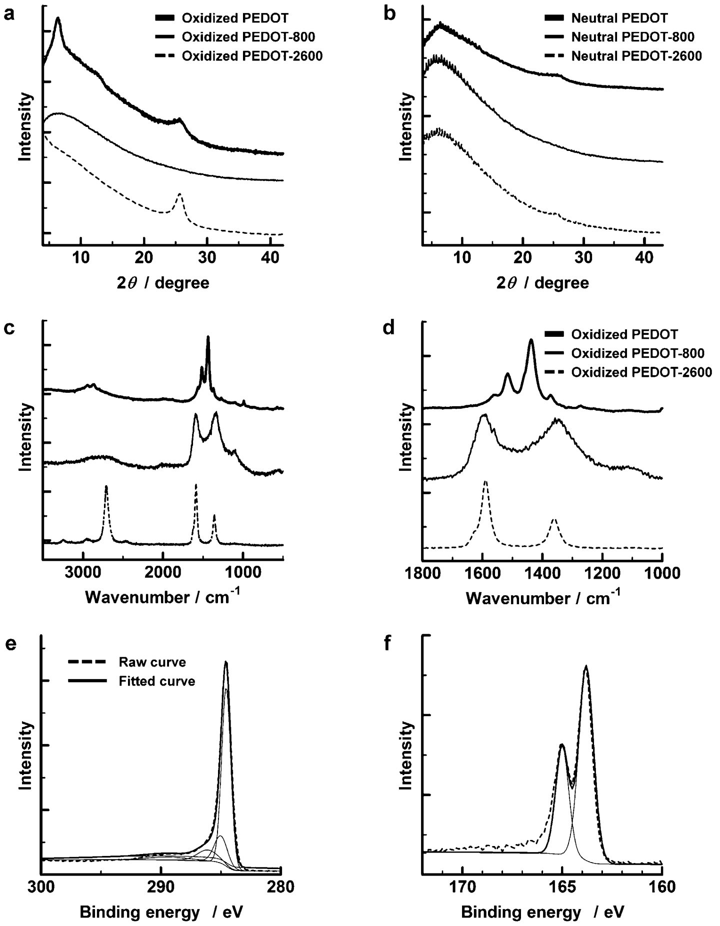


Figure 3. XRD patterns of a) oxidized and b) neutral PEDOT, carbon, and graphite films. c) Raman scattering spectra of oxidized PEDOT, carbon, and graphite films, and d) their magnified spectra. High-resolution e) C 1s and f) S 2p XPS spectra of the oxidized PEDOT-800 film.

tively. The main peak of the C 1s spectrum at 284.6 eV is assigned to sp^2 carbon atoms, suggesting that the networks of sp^2 carbon bonds are formed to some extent.[16] The subpeaks at higher binding energy indicate the existence of carbon atoms bonding to sulfur and oxygen atoms. The S 2p spectrum can be deconvoluted into two clear peaks at 163.8 and 165.0 eV corresponding to S $2p_{3/2}$ and S $2p_{1/2}$ of thiophenic sulfur, respectively. Thus, it can be inferred that the sulfur is mainly found in thiophene-like structures in the carbon material. This result is reasonable by taking account of the molecular structure of the precursor.[17] The atomic percentage of oxygen, carbon, and sulfur of the oxidized PEDOT-800 film is 2.06, 95.22, and 2.72 %, respectively. A clear difference in the quantitative sulfur content and bonding states of sulfur between the neutral and oxidized PEDOT-800 films was not observed.

Interestingly, the helical morphology of the oxidized H-PEDOT film remained unchanged after the carbonization at 800 °C. A spiral morphology consisting of fibril bundles is observed in a domain. The helical carbon films prepared using the (*R*)- and (*S*)-PEDOT films exhibit spiral morphologies with left- and right-hand screw directions, respectively (Figure 4 a and b). Therefore, it can be argued that the helical senses of the spirals consisting of carbon fibrils are controllable by choosing the chirality of the chiral dopant. The distance between the fibril bundles was 130 nm. The morphologies of the H-PEDOT films synthesized in N*-LCs of systems 1 and 2 were also preserved even after the carbonization (Figures S9 and S10). The morphology-retaining carbonization is possible not only for the oxidized H-PEDOT film but also for the neutral H-PEDOT film bearing almost no ClO_4^- dopant (Figure 4 c). This is quite different from the carbonization of a PA film, where the use of an oxidized film obtained from iodine doping is required for the morphology-retaining carbonization.[2] This is due to the infusibility of the PEDOT films at high temperature, which is characteristic of aromatic π-conjugated polymers with rigid backbone. Figure 4 d shows a SEM image of the oxidized H-PEDOT-2600 film that was prepared using the N*-LC of system 3 including the chiral dopant of (*R*)-D2. It should be emphasized that the graphite film prepared by the heat treatment at 2600 °C has almost the same surface morphology as that of the original H-PEDOT film and that of the helical carbon film prepared at 800 °C, except for a thermal shrinkage.

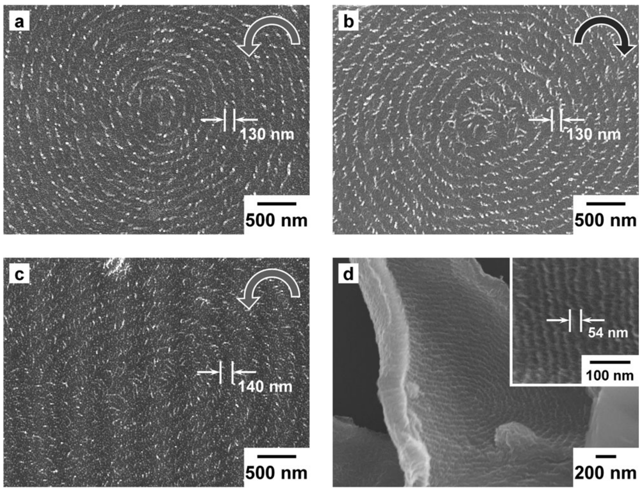


Figure 4. SEM images of the oxidized H-PEDOT-800 films with spiral morphologies that were prepared using the a) (*R*)- and b) (*S*)-N*-LCs of system 3, respectively [5CB:(*R*)- or (*S*)-D2:bis-EDOT:T-BAP = 100:1:3:0.5]. c) SEM image of the neutral H-PEDOT-800 film that was prepared using N*-LC of system 3 including (*R*)-D2. d) SEM image of the oxidized H-PEDOT-2600 film that was prepared using the (*R*)-N*-LC of system 3.

It is generally difficult to prepare undoped and neutral PEDOT through electrochemical synthesis.[18] This is because the dedoping of the oxidized PEDOT film cannot be completely achieved, as mentioned above. Here, it is desirable to compare the present neutral and oxidized PEDOT films with the "entirely neutral PEDOTs", which can be prepared by another synthesis method, in terms of feature, structure, and thermal behavior in carbonization. The entirely neutral PEDOT was synthesized through dehalogenation polycondensation in an isotropic solvent instead of the electrochemical oxidative polymerization.[19] The polymer was obtained in powder form and was found to be insoluble in regular organic solvents. The carbon particles obtained from the neutral PEDOT at 800 °C showed slightly better crystallinity than that of the PEDOT-800 films with an amorphous structure (Figure 3 a,b, and Figure S11). The difference in the degree of crystallinity between the carbonized materials may be attributed to the difference in hydrogen content and in the polymerization methods used to synthesize the corresponding precursor polymers (for details see the Supporting Information). Finally, although the entirely neutral PEDOTs could be potentially useful carbonization precursors, especially in terms of the degree of crystallinity, they are not able to produce helical graphite or even carbon films. Therefore, among the three types of PEDOTs (oxidized PEDOT film, neutral PEDOT film, and entirely neutral PEDOT), the oxidized PEDOT films are the most promising precursors for the preparation of helical carbon and graphite films.

In summary, we found that the oxidized PEDOT films consisting of closely packed polymer chains, which are stabilized by the electrostatic interaction between the cationic polymer chain and the anionic dopant, perform effective carbonization, leading to the highly crystalline graphite films. It was also demonstrated that the carbonization of a helical aromatic π-conjugated polymer film with a tunable helical sense and degree of helicity is a promising approach for the preparation of hierarchically controlled helical carbon and graphite films. The present helical carbon atoms might exhibit unique electrochemical properties characteristic of the helical structure. The induced solenoid magnetism, based on high electrical conductivity and well-controlled helical structure, might be one of the most anticipated and outstanding properties of helical graphites.

Experimental Section

The molecular structures of the chiral dopants, the N-LC, the supporting electrolyte (tetra-*n*-butylammonium perchlorate;

TBAP), and the monomer are depicted in Scheme S1. Di- and tetrasubstituted axially chiral binaphthyl derivatives were synthesized as described in previous reports.[13,20] The former is (*R*)- or (*S*)-2,2′-PCH506-1,1′-binaphthyl [abbreviated as (*R*)- or (*S*)-D1]; the latter is (*R*)- or (*S*)-2,2′-PCH5012-6,6′-PCH5-1,1′-binaphthyl [abbreviated as (*R*)- or (*S*)-D2].

The helical twisting powers of the chiral dopants, the concentration ratios, and the helical pitches of the N*-LCs are summarized in Table S1. 5CB was used as a parent LC for the N*-LC. The N*-LC of system 1 was prepared by adding 1 mol% of the chiral dopant, D1, into 5CB. The N*-LCs of systems 2 and 3 were prepared by adding 0.5 and 1 mol% of D2 into the N-LC, respectively.

The electrochemical polymerizations in asymmetric reaction fields were performed using the N*-LCs for the production of H-PEDOT films. The N*-LC solutions were prepared by adding 0.5–1 mol% of D1 or D2, 3 mol% of bis-EDOT, and 0.5 mol% of TBAP into 5CB. The full experimental details of the polymerization methods are presented in the Supporting Information. The H-PEDOT films for the measurements of UV/Vis and CD spectra were synthesized in the N*-LC solutions that were prepared by adding 0.5–2 mol% of D1 or D2, 2 mol% of bis-EDOT, and 0.2 mol% of TBAP into 5CB. The dedoping process was performed by applying 4 V to the H-PEDOT films in an acetonitrile (MeCN) solution of TBAP (0.05 M) for five minutes at room temperature.

The PEDOT film was carbonized at 800°C using the electric furnace for 1 h with a heating rate of 10°C min^{-1}. The carbonized film was furthermore heated at 2600°C with a graphitizing apparatus for 30 minutes in flowing argon gas.

Received: September 28, 2013
Revised: November 14, 2013

Keywords: chirality · electrochemistry · helical structures · liquid crystals · polymerization

---

[1] K. E. Shopsowitz, W. Y. Hamad, M. J. MacLachlan, *Angew. Chem.* **2011**, *123*, 11183 – 11187; *Angew. Chem. Int. Ed.* **2011**, *50*, 10991 – 10995.

[2] a) M. Kyotani, S. Matsushita, T. Nagai, Y. Matsui, M. Shimomura, A. Kaito, K. Akagi, *J. Am. Chem. Soc.* **2008**, *130*, 10880 – 10881; b) S. Matsushita, M. Kyotani, K. Akagi, *J. Am. Chem. Soc.* **2011**, *133*, 17977 – 17992.

[3] K. Akagi, *Chem. Rev.* **2009**, *109*, 5354 – 5401.

[4] a) L. B. Groenendaal, F. Jonas, D. Freitag, H. Pielartzik, J. R. Reynolds, *Adv. Mater.* **2000**, *12*, 481 – 494; b) K.-R. Lee, G. A. Sotzing, *Chem. Commun.* **2013**, *49*, 5192 – 5194.

[5] S. Matsushita, K. Akagi, *Isr. J. Chem.* **2011**, *51*, 1075 – 1095.

[6] a) H. Goto, K. Akagi, *Macromol. Rapid Commun.* **2004**, *25*, 1482 – 1486; b) H. Goto, *J. Mater. Chem.* **2009**, *19*, 4914 – 4921; c) Y. S. Jeong, K. Akagi, *Macromolecules* **2011**, *44*, 2418 – 2426; d) S. Matsushita, Y. S. Jeong, K. Akagi, *Chem. Commun.* **2013**, *49*, 1883 – 1890.

[7] CD measurements were performed through the rotation of the sample to exclude both the artifact and linear polarization in the Cotton effect.

[8] “Exciton Chirality Method: Principles and Applications”: N. Berova, K. Nakanishi in *Circular Dichroism: Principles and Applications*, 2nd ed. (Eds.: N. Berova, K. Nakanishi, R. Woody), Wiley, New York, **2000**; chap. 12, pp. 337 – 382.

[9] T. Mori, M. Kyotani, K. Akagi, *Macromolecules* **2010**, *43*, 8363 – 8372.

[10] P. Leriche, P. Blanchard, P. Frère, E. Levillain, G. Mabon, J. Roncali, *Chem. Commun.* **2006**, 275 – 277.

[11] a) J. Huang, S. Virji, B. H. Weiller, R. B. Kaner, *J. Am. Chem. Soc.* **2003**, *125*, 314 – 315; b) X. Zhang, S. K. Manohar, *J. Am. Chem. Soc.* **2004**, *126*, 12714 – 12715; c) X. Zhang, A. G. MacDiarmid, S. K. Manohar, *Chem. Commun.* **2005**, 5328 – 5330.

[12] K. Akagi, S. Guo, T. Mori, M. Goh, G. Piao, M. Kyotani, *J. Am. Chem. Soc.* **2005**, *127*, 14647 – 14654.

[13] M. Goh, M. Kyotani, K. Akagi, *J. Am. Chem. Soc.* **2007**, *129*, 8519 – 8527.

[14] Since the H-PEDOT films were too thin to obtain a sufficient amount for reliable characterizations, freestanding PEDOT films were electrochemically synthesized in MeCN as an isotropic solvent instead of a N*-LC solution under similar conditions. The obtained PEDOT films were then carbonized and subsequently graphitized, yielding the freestanding PEDOT-800 and PEDOT-2600 films, respectively. The neutral and oxidized PEDOT, PEDOT-800, and PEDOT-2600 films were characterized in terms of thermal, structural, and electrical properties by elemental analysis, SEM, IR spectroscopy, thermogravimetric analysis, XRD, XPS, Raman spectroscopy, and electrical conductivity. Details can be found in the Supporting Information.

[15] K. E. Aasmundtveit, E. J. Samuelsen, O. Inganäs, L. A. A. Pettersson, T. Johansson, S. Ferrer, *Synth. Met.* **2000**, *113*, 93 – 97.

[16] S. Stankovich, R. D. Piner, X. Chen, N. Wu, S. T. Nguyen, R. S. Ruoff, *J. Mater. Chem.* **2006**, *16*, 155 – 158.

[17] J. P. Paraknowitsch, A. Thomas, J. Schmidt, *Chem. Commun.* **2011**, *47*, 8283 – 8285.

[18] *PEDOT: Principles and Applications of an Intrinsically Conductive Polymer* (Eds.: A. Elschner, S. Kirchmeyer, W. Lövenich, U. Merker, K. Reuter), CRC, Boca Raton, **2011**, chap. 6, pp. 67 – 81.

[19] a) T. Yamamoto, A. Morita, Y. Miyazaki, T. Maruyama, H. Wakayama, Z. Zhou, Y. Nakamura, T. Kanbara, S. Sasaki, K. Kubota, *Macromolecules* **1992**, *25*, 1214 – 1223; b) T. Yamamoto, M. Abla, *Synth. Met.* **1999**, *100*, 237 – 239.

[20] K. Akagi, G. Piao, K. Kaneko, K. Sakamaki, H. Shirakawa, M. Kyotani, *Science* **1998**, *282*, 1683 – 1686.