Formation of Chiral, Three-Dimensional Aggregates by Self-Assembly of Helical Components

Mila Boncheva, Derek A. Bruzewicz, and George M. Whitesides*

Department of Chemistry and Chemical Biology, Harvard University, Cambridge, Massachusetts 02138

This work describes the self-assembly of millimeter-sized helical components—fabricated by replica molding from sections of drill bits and bolts—into 3D aggregates via capillary forces. The components form aggregates of different geometry: components derived from drill bits formed regular helices, and those derived from bolts formed irregular warped sheets. Enantioselective interactions between components derived from drill bits resulted in the formation of aggregates with complex structures, including enantiomerically pure helices, aggregates with multiple helical segments, and chiral aggregates formed from achiral components, i.e., spheres.

Introduction

This work examines the self-assembly of helical, millimeter-sized components into three-dimensional (3D) aggregates. We address the design of the components and identify some of the requirements they must meet to form chiral aggregates. In analogy to molecular recognition, we use enantioselective capillary interactions between the components and demonstrate the formation of aggregates with complex structures, including helices of defined chirality, aggregates with multiple helical segments, and chiral structures composed of achiral components, i.e., spheres.

Self-assembly[1] of 3D structures from mesoscale (nanometer-to-millimeter-sized) components is a useful strategy for generating structured[2–5] and functional[6–12] aggregates of components too small or too numerous to be manipulated individually. In order for self-assembly to compete with other, more familiar methods for generating complex structures (e.g., pick-and-place assembly[13]), it must show the potential to generate structures that these methods cannot. One set of targets includes 3D, chiral, and asymmetrical aggregates of small components (0.1–10 μm); these aggregates may be useful in photonic[14] and subwavelength[15] optical applications and in devices with electrical connectivity or microelectronic function.[1]

Self-assembly of millimeter-sized components provides a useful model system with which to examine this type of self-assembly. We believe that the principles of self-assembly at the millimeter scale can, in many cases, be extended to micrometer-sized components. Components with sizes of a few millimeters can be easily fabricated, and the products of their self-assembly can be easily examined by eye.[1] Millimeter-scale self-assembled systems have, with few exceptions,[4,16,17] used achiral components that interact through planar surfaces; the resulting aggregates have had achiral, periodic structures exhibiting high symmetry. In contrast, molecular self-assembly and organic synthesis routinely use chirality to increase the structural diversity and complexity of the resulting aggregates;[18] self-assembly in molecular systems is often based on interactions between complementary 3D surfaces. In this work, we explored the self-assembly of millimeter-sized components interacting through chiral, 3D surfaces.

Experimental Design

The chiral components used in this work were short segments of a helix (Figure 1). We chose a helical shape for three reasons: (i) The helix is a familiar chiral motif, widely found in self-assembling systems of molecules. (ii) Helices offer simple examples of shape complementarity, with the ridge of one piece fitting into the groove of another. The chirality of the helix can be used to provide selectivity in a set of mixed components. (iii) Helical components with different parameters characterizing the helix (e.g., helical angle, width of the grooves) can be fabricated easily by replica molding starting with metal masters cut from drill bits and bolts.[19]

* Corresponding author: telephone, 617-495-9430; telefax, 617-495-9857; e-mail, gwhitesides@gmwgroup.harvard.edu.

(1) Whitesides, G. M.; Boncheva, M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4769.

(2) Klimov, V. I.; Mikhailovski, A. A.; Xu, S.; Malko, A.; Hollingsworth, J. A.; Leatherdale, C. A.; Eisler, H.-J.; Bawendi, M. G. *Science* **2000**, *290*, 314.

(3) Sun, S. H.; Murray, C. B.; Weller, D.; Folks, L.; Moser, A. *Science* **2000**, *287*, 1989.

(4) Breen, T. L.; Tien, J.; Oliver, S. R. J.; Hadzic, T.; Whitesides, G. M. *Science* **1999**, *284*, 948.

(5) Clark, T. D.; Tien, J.; Duffy, D. C.; Paul, K.; Whitesides, G. M. *J. Am. Chem. Soc.* **2001**, *123*, 7677.

(6) Cohn, M.; Kim, C. J.; Pisano, A. In *Proceedings Transducers '91 International Conference on Solid-State Sensors and Actuators*; IEEE: New York, 1991; p 493.

(7) Yeh, H.-J. J.; Smith, J. S. *IEEE Photon Technol. Lett.* **1994**, *6*, 706.

(8) Harsh, K. F.; Bright, V. M.; Lee, Y. C. *Sens. Actuators, A* **1999**, *77*, 237.

(9) Syms, R. R. A. *IEEE Photon Technol. Lett.* **2000**, *12*, 1519.

(10) Srinivasan, U.; Liepmann, D.; Howe, R. T. *J. Microelectromech. Syst.* **2001**, *10*, 17.

(11) Boncheva, M.; Gracias, D. H.; Jacobs, H. O.; Whitesides, G. M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4937.

(12) Jacobs, H. O.; Tao, A. R.; Schwartz, A.; Gracias, D. H.; Whitesides, G. M. *Science* **2002**, *296*, 323.

(13) Boehringer, K. F.; Fearing, R. S.; Goldberg, K. Y. In *The Handbook of Industrial Robotics*, 2nd ed.; Nof, S., Ed.; John Wiley and Sons: New York, 1999; p 1045.

(14) Yablonovitch, E. *Sci. Am.* **2001**, *285*, 46.

(15) Vijayalakshmi, S.; Zhang, Y.; Yaglioglu, G.; Dorsinville, R.; White, C. W.; Grebel, H. *Springer Ser. Chem. Phys.* **2001**, *66 (Ultrafast Phenomena XII)*, 171.

(16) Oliver, S. R.; Clark, T. D.; Bowden, N.; Whitesides, G. M. *J. Am. Chem. Soc.* **2001**, *123*, 8119.

(17) Gracias, D. H.; Boncheva, M.; Omoregie, O.; Whitesides, G. M. *Appl. Phys. Lett.* **2002**, *80*, 2802.

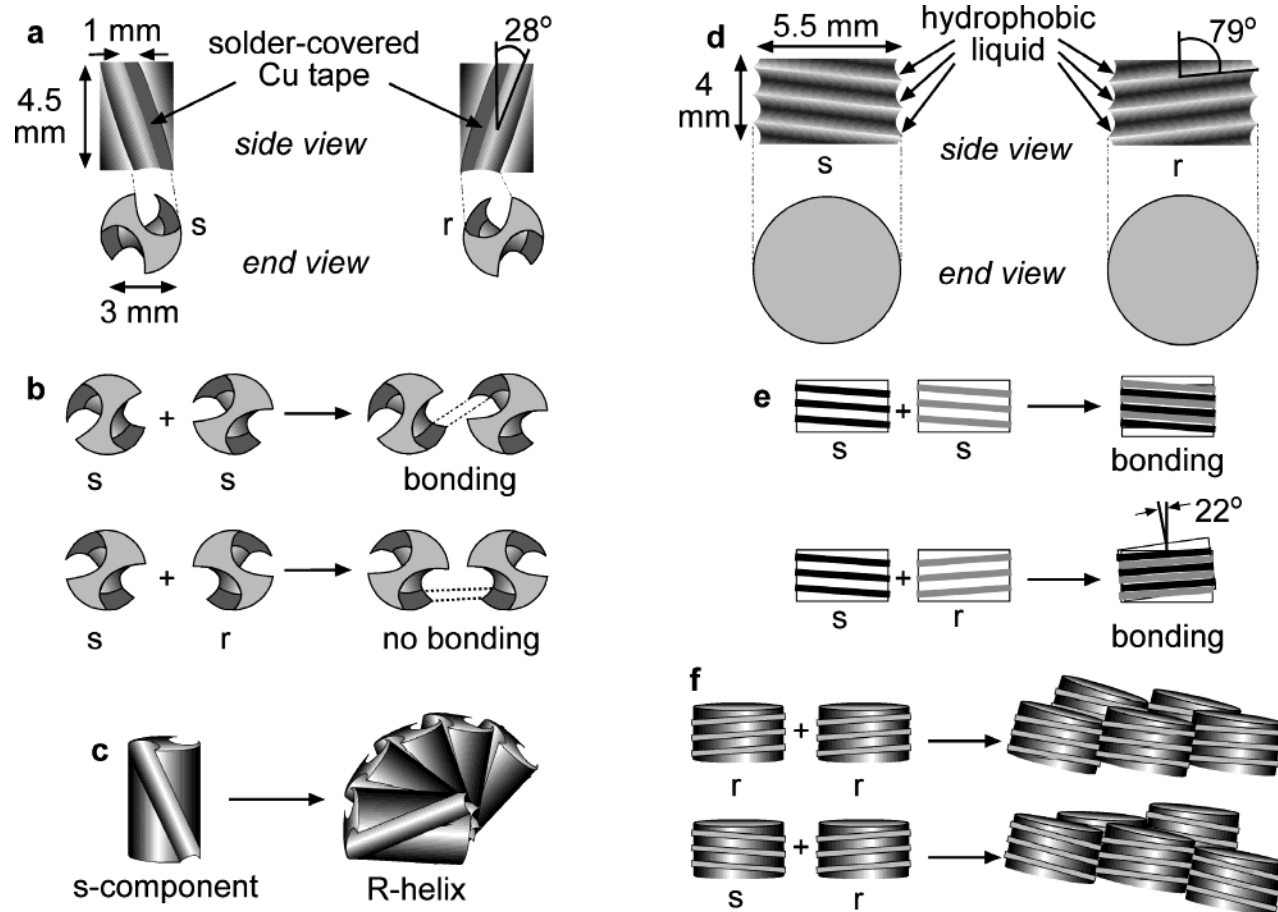(18) Lehn, J.-M. *NATO ASI Ser., Ser. E* **1996**, *320*, 511.

Figure 1. Helical components used: (a) schematic representation of components derived from left-handed (s) and right-handed (r) drill bits; (b) scheme describing the interaction between two components derived from drill bits of the same (top) and opposite (bottom) chirality; (c) formation of a right-handed helix (R) from components derived from left-handed drill bits; (d) schematic representation of components derived from left-handed (s) and right-handed (r) bolts; (e) interaction between two components derived from bolts of the same (top) and opposite (bottom) chirality; (f) formation of aggregates from components derived from bolts of the same (top) and opposite (bottom) chirality.

The helices in drill bits and bolts have different geometries. Drill bits are double helices. They have wider ridges than grooves, and a relatively low helical angle—defined as the angle between the long axis of the helix and the grooves (Figure 1a). This geometry and the dimensions of the components we used dictate that two sections of a drill bit can fit together—ridge-in-groove—only if they meet three conditions: they are of the same chirality, they contain not more than one-fourth of a turn of a helix, and their long axes are rotated in-plane by approximately 28° (Figure 1b). Each component derived from a drill bit can interact with only two other components. These constraints on the self-assembly of components derived from drill bits result in the formation of linear helices with a pitch of 11 pieces per turn (Figure 1c).

In contrast, bolts are single helices. They have grooves and ridges of identical width, and relatively high helical angle (Figure 1d). The sides of the components shaped as bolts can be approximated simply as parallel ridges, so that two such components of unlimited length can fit together ridge-in-groove. Components of opposite chirality can bind each other as easily as those of the same chirality, because tilting the longitudinal axes of components of opposite chirality—in our case, by approximately

22°—positions their ridges and grooves parallel to each other (Figure 1e). This type of association can lead to formation of aggregates of mixed chirality (Figure 1f). Each component can interact with up to six other components; this type of binding results in formation of hexagonally packed aggregates.

Self-assembly in the system we describe was based on two types of capillary interactions:[17] (i) The strong interaction between drops of molten solder was used with components molded on drill bits. (The free energy of the water–solder interface is ~400 ergs/cm^2.)[4] (ii) The relatively weak capillary interaction between drops of hydrophobic, photocurable liquid was used with components molded on bolts, since patterning these components with molten solder would have been difficult. (The free energy of the hydrophobic liquid–water interface is ~50 ergs/cm^2.)[20] In both cases, the liquid drops were patterned selectively into the chiral grooves of the components. When the components were suspended in water, and droplets of liquid (adhesive or metal) on two pieces came into contact, these droplets fused; this fusion minimized the area, and thus the interfacial free energy, of the liquid/water interface. Hardening the liquid, either by cooling the solder or curing the hydrophobic adhesive, generated mechanically stable structures.

(19) Right- and left-handed drill bits and bolts are commercially available in a variety of sizes and helical angles (see, for example, http://advantage-drillbits.com); the fabrication of chiral masters of different geometry (e.g., polyhedra with chirally differentiated shapes[4, 16] or chirally patterned faces[10,11]) entails custom fabrication.

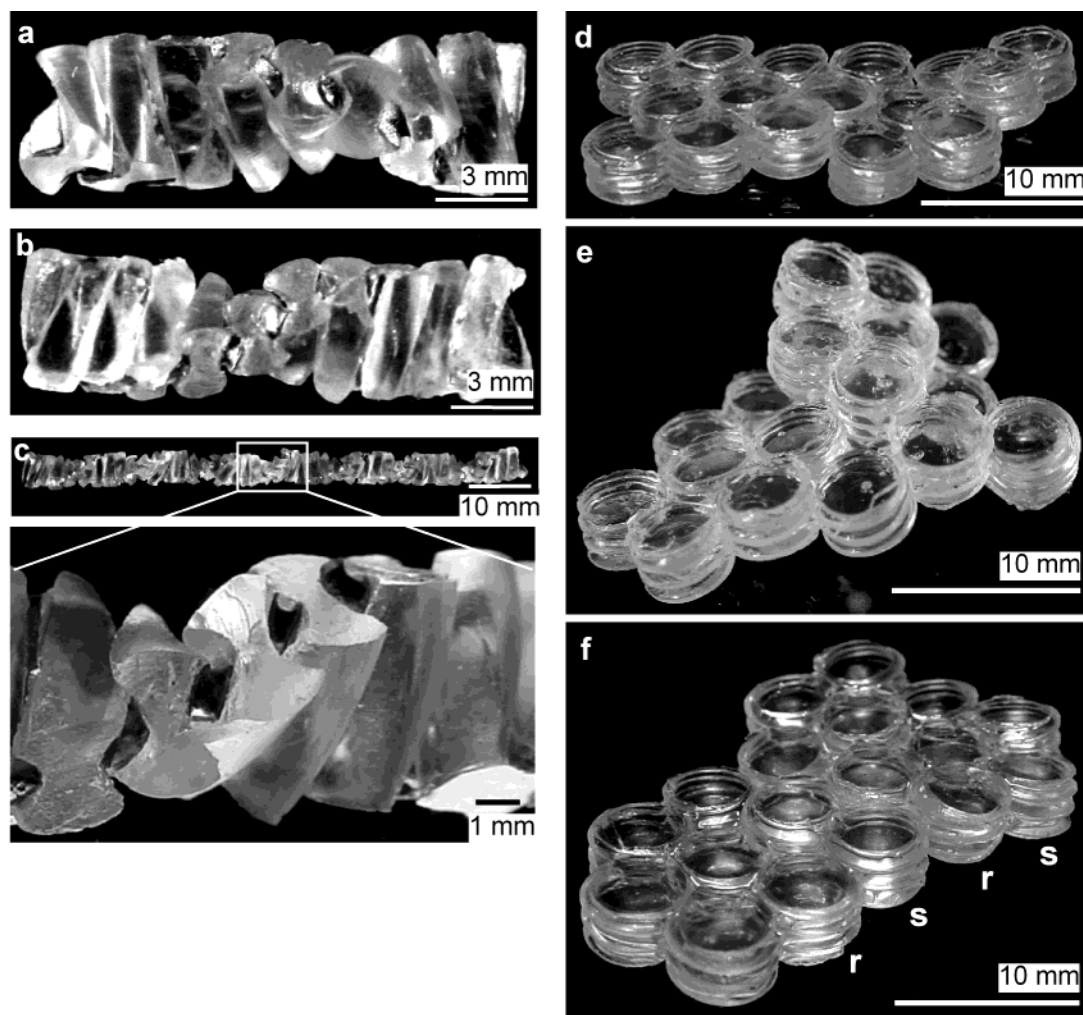(20) Tien, J.; Breen, T. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1998**, *120*, 12670.

Figure 2. Photographs of aggregates self-assembled from components derived from drill bits (a−c) and bolts (d−f): (a, b) right-handed (R) and left-handed (L) helices, self-assembled from 45 left-handed (a) or right-handed (b) components in a 300 mL spherical Morton flask with a diameter of 55 mm; (c) L-helix self-assembled from the same number of components in a cylindrical 50-mL Morton flask with a width of 23 mm; (d, e) warped sheet aggregates self-assembled from 30 left-handed (d) or right-handed (e) bolt-shaped components; (f) an aggregate formed by self-assembly of 20 left-handed and 20 right-handed bolt-shaped components.

Results and Discussion

Fabrication and Self-Assembly. We fabricated the components using modifications of procedures described previously. The Experimental Section gives details.

Aggregates from Components Derived from Drill Bits. These components assembled into helical aggregates, with the edge of the ridge of one component fitting into part of the groove of another component (Figure 1c). The chirality of the grooves determined the chirality of the aggregates: pieces molded from left-handed drill bits assembled into right-handed helices, and vice versa. A "racemic" mixture of right- and left-handed drill bits spontaneously segregated into left- and right-handed helices. Results did not vary with the size of the components, as long as each component contained no more than one-quarter of a helical turn.

When the self-assembly was carried out in a large volume of suspending liquid, shear broke up large aggregates. By using containers shaped to limit the volume available to the components during assembly, and thereby to minimize shear, it was possible to make larger aggregates. Panels a−c of Figure 2 show examples of aggregates formed from a total of 45 pieces using containers of different volume and geometry. When the assembly was carried out in a spherical Morton flask of volume 300

mL and a diameter of 55 mm, the system stabilized into several 7- to 12-mer helical segments (Figure 2a,b). Assembly of the same number of components performed in a cylindrical 50-mL Morton flask with a width of 23 mm resulted in a single 45-mer aggregate (Figure 2c). The time required for completion of the assembly depended on the number of components incorporated into the final aggregate: it was 15−30 min for the short aggregates, and 4−5 h for the long aggregate.

Aggregates from Components Derived from Bolts. These components formed irregular, sheetlike aggregates (Figure 2d,e). Adjacent pieces in the aggregates had parallel axes, parallel threads, or any orientation in between. As a result, some parts of the aggregates were nearly flat, while others were warped. As expected from their geometry (see Figure 1e), self-assembly of a mixture of left- and right-handed pieces resulted in formation of mixed aggregates (Figure 2f). These results did not vary with the number of helical turns in the components.

Our results allow us to make two points concerning the generation of chiral aggregates. First, a chiral aggregate can result either from chiral, planar patterns, through which the components interact, or from chiral 3D shapes of the surfaces to which these patterns are attached. We have previously demonstrated formation of chiral 3D
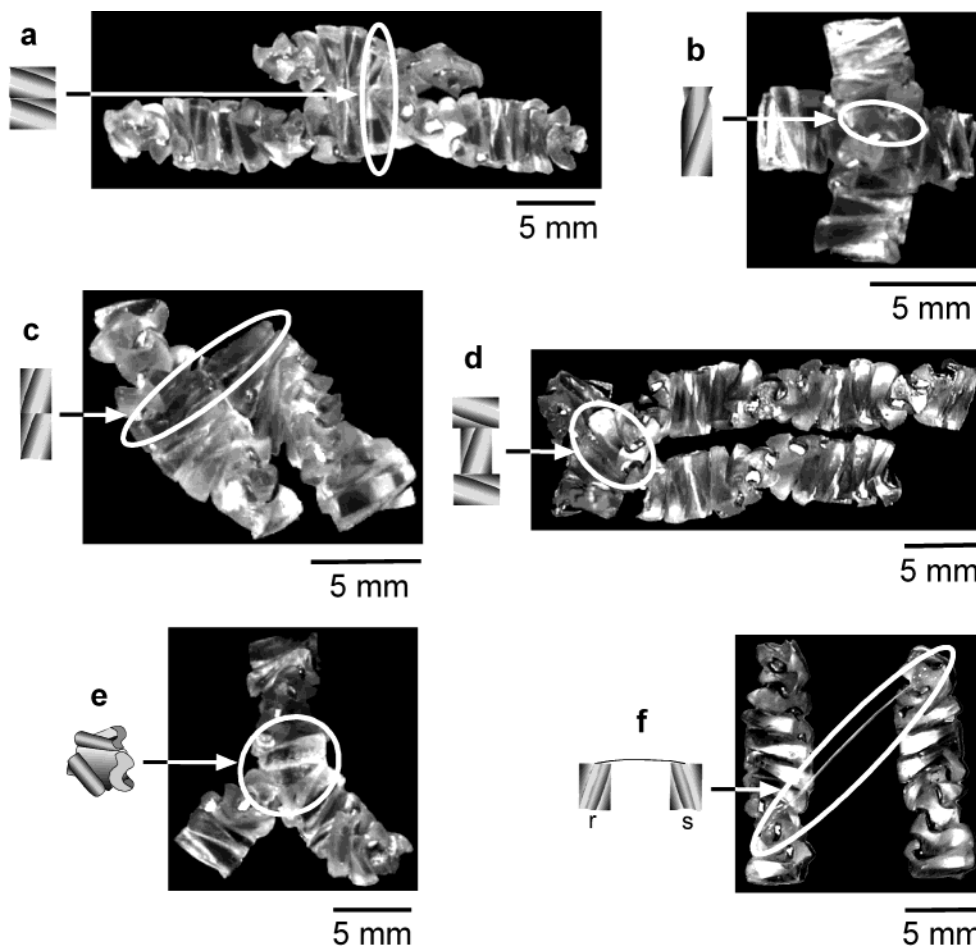
Figure 3. Chiral aggregates with complex topography self-assembled by growth from kernels. The structure of the kernel used in each case is schematically shown to the left of each photograph. The kernels used in (**a**−**d**) were fabricated by gluing together right-handed (r) components derived from drill bits with polyurethane. The three r-components in (**e**) were glued around a triangular carrier piece made of PDMS. The r- and s-components in (**f**) were linked together using a polyurethane linker of length 16 mm and thickness 200 μm. All assemblies were performed in a round-bottomed, cylindrical, Morton flask with a volume of 150 mL. The time required for completion of the assembly was approximately 1 h in all cases.

aggregates from components interacting through chirally patterned planar surfaces.[16] The components derived from drill bits interacted through patterns attached to 3D chiral grooves; they assembled into chiral aggregates. Second, when the components interact through chiral 3D surfaces, chirality of these surfaces is not sufficient to ensure chirality of the aggregates; a high degree of shape complementarity between the interacting surfaces is also required. The components derived from bolts interacted through shallow, chiral grooves and ridges; they assembled into irregular, achiral aggregates. In contrast, the components derived from drill bits interacted through considerably deeper chiral grooves and ridges; they assembled into regular, chiral aggregates.

The ability to use either (or both) type of design for recognition elements—planar or 3D—offers useful freedom when designing systems of self-assembling chiral components. The design can provide a compromise between the difficulty of fabrication of the components and the complexity of the system: it is often easier to fabricate and functionalize components with planar surfaces than it is to functionalize components with chiral shapes; components interacting via 3D chiral surfaces, however, can be used to design more sophisticated self-assembling systems—e.g., systems employing shape complementarity in addition to enantiomeric recognition—than can achiral self-assembly.

Assembly of Chiral Aggregates with Complex Topography. Each helical assembly of components derived from drill bits grew from a dimer. By preassembling components into n-mers ($n = 2-4$) with defined structures ("kernels"), we were able to form self-assembled aggregates comprising several helical segments (Figure 3).

This type of chiral self-assembly was also used to template the formation of chiral structures from nonchiral components, i.e., spheres (Figure 4). Two Delrin (polyoxymethylene homopolymer) spheres were glued using Pronto CA-50 Gel adhesive (3M Company) to each end of components molded on drill bits (Figure 4a). Self-assembly of these modified components generated helices (Figure 4b). Thermal annealing above the glass transition temperature of the Delrin ($T_g = 340$ °C) joined the adjacent spheres. After this fusion, we connected the spheres at the ends of opposed chains with molten Delrin manually. Dissolution of the chiral components (CH_2Cl_2, 40 min) released a free-standing, double-helical structure consisting of fused Delrin spheres (Figure 4c). The strips of polyimide/copper composite, which carried the patterns of solder, did not dissolve and settled at the bottom of the glass container.

Conclusions

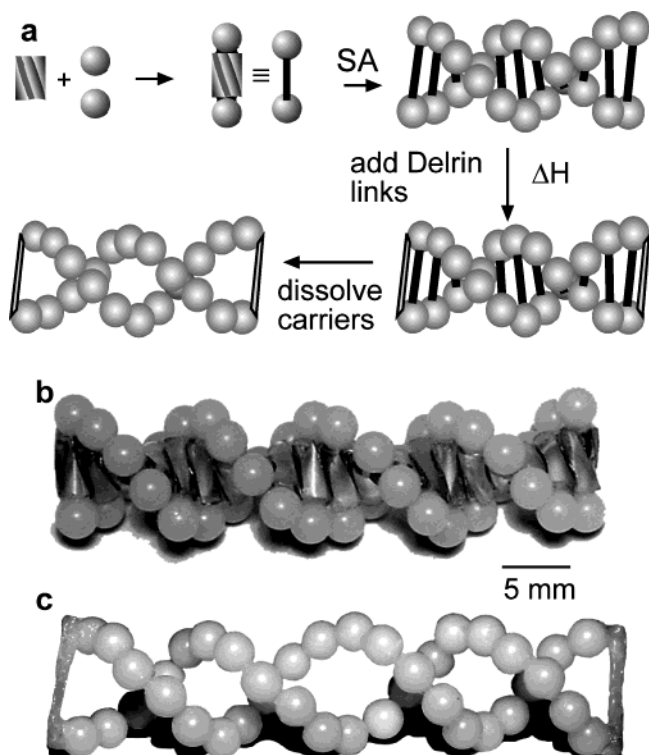This work demonstrates the self-assembly of millimeter-scale helical components into new types of structures. The

Figure 4. Self-assembly of a free-standing double helix of spheres. **(a)** Scheme of the experimental strategy. **(b)** Photograph of the right-handed helix assembled from 20 components derived from left-handed drill bits. The assembly was performed in a cylindrical 50-mL Morton flask with a width of 23 mm. The time required for completion of the self-assembly was approximately 2 h. **(c)** Photograph of the free-standing double helix of spheres. The structure was obtained after immersion of the aggregate shown in **(b)** in CH_2Cl_2 for 40 min.

system was designed based on concepts—shape complementarity, helicity, and enantioselectivity—familiar from molecular recognition.[21] We were able to control the shape, size, and complexity of the self-assembled 3D aggregates by using the shape of the chiral components, by the volume and shape of the space available to them during self-assembly, and, in some cases, by the design of the structures used to nucleate growth of complex aggregates.

The effectiveness of the two strategies we have used—self-assembly of components derived from drill bits and from bolts—differs considerably. Our results show that the formation of regular, chiral aggregates from components that interact via 3D surfaces is possible only when two conditions are met: (i) the interacting surfaces of the components are chiral and (ii) the interacting surfaces have a high degree of shape complementarity—that is, the components must be able to assume a unique relative orientation in an aggregate. The components derived from drill bits met both conditions, and their self-assembly resulted in formation of interesting and topologically complex aggregates. The components derived from bolts did not meet the second condition (high degree of shape complementarity), and were, therefore, unsuitable for self-assembly of chiral 3D aggregates.

The self-assembling system we described is a useful model system with which to study the conditions leading to formation of structurally complex, 3D aggregates. A strategy based on self-assembly of 10^2-10^3 times smaller components than those used here would offer routes to

new types of structures with optical or electronic functionality.[1] The principle limitation to self-assembly using helical components in the micrometer-size regime is the fabrication of the individual components. The millimeter-sized helices we used were fabricated serially (one at the time) using a tedious manual procedure. Helical components with diameters as small as 100 μm can, in principle, be fabricated as described here, by molding using commercially available drill bits[22] as masters. Further reduction in the dimensions of the components would require more sophisticated fabrication procedures. For example, we have previously demonstrated fabrication of helical wires with a pitch of 25 μm on a cylinder with diameter of 100 μm using soft lithography.[23] Inorganic conducting helical fibers with diameters ranging from 30 μm to millimeters, and lengths of up to 25 cm, can form spontaneously from uniform sols.[24] A strategy for functionalizing the surfaces of micrometer-sized helical components to allow their self-assembly has not yet been developed. One possible strategy could, in principle, be based on electrochemical modification of the interacting surfaces, e.g., electrodeposition of solder.[25,26]

Experimental Section

Fabrication of the Components. We fabricated the millimeter-sized components by replica molding using right- and left-handed drill bits and bolts as masters. Pieces of length 4.5 mm and 4 mm were cut from stainless steel drill bits and bolts, respectively, placed in polyethylene dishes (with their axes perpendicular to the bottom of the dish), and covered with poly-(dimethylsiloxane) (PDMS) prepolymer (Sylgard 184, Dow Corning). After the prepolymer was cured thermally for 3 h at 60 °C, the metal masters were removed and the resulting molds were used to replicate components. The molds were filled with photocurable polyurethane (PU) prepolymer (J-91, Summers Optical Labs) and cured under UV light (100 W, mercury lamp) for 1 h. The resulting PU helical components were functionalized for self-assembly.

For components generated from drill bits, we cut rectangular stripes of polyimide—copper laminate (Pyralux LF 9110, DuPont) manually to size (1 mm width, 4.5 mm length), and glued them into the helical groves using Pronto CA-50 Gel adhesive (3M Company). The components were then dipped into molten solder (Bi–Pb–Sn–Cd–In alloy, T_m 47 °C, Small Parts, Inc.); the solder selectively wetted the stripes of copper. For components generated from bolts, we covered the threaded faces with nail polish (CoverGirl Peelers, Procter & Gamble), and oxidized the pieces in N_2 plasma for 1 min. The nail polish was removed by peeling. The plasma treatment rendered the exposed top and bottom flat faces of the components hydrophilic, while the protected threads remained hydrophobic.

Self-Assembly of Components Derived from Drill Bits. These components were placed in a Morton flask filled with an approximately isodense aqueous solution of KBr at a temperature above the melting point of the solder (60 °C). The acidity of the solution was lowered to pH = 3 with acetic acid to dissolve oxides formed on the solder surface. A small amount of detergent was added (Triton X 100, approximately 10 μL/L of H_2O) to prevent the formation of bubbles during assembly. Upon rotation of the container using the motor of a rotary evaporator (rate of rotation ~30 rpm), the components collided. Fusion of the drops of molten solder drove the self-assembly of the components into aggregates. After self-assembly was complete and the rotation stopped, cooling the aqueous suspension to room temperature allowed the solder to harden and yielded mechanically stable structures.

(21) Alberts, B.; Bray, D.; Lewis, J.; Raff, M.; Roberts, K.; Watson, J. D. *Molecular Biology of the Cell*, 3rd ed.; Garland: New York, 1994.

(22) Drill bits with diameter of 100 μm are commercially available from Topoint Technology Co., Ltd., Taipei Hsien, Taiwan.
(23) Jackman, R. J.; Brittain, S. T.; Adams, A.; Prentiss, M. G.; Whitesides, G. M. *Science* **1998**, *280*, 2089.
(24) Giraldo, O.; Brock, S. L.; Marquez, M.; Suib, S. L.; Hillhouse, H.; Tsapatsis, M. *Nature* **2000**, *405*, 38.
(25) Annala, P.; Kaitila, J.; Salonen, J.; Suni, I. *NATO ASI Ser., Ser.3: High Technol.* **1998**, *54*, 81.
(26) Lin, K.-L.; Hsu, K.-T. *Plating Surf. Finishing* **2000**, *87*, 86.

Self-Assembly of Components Derived from Bolts. Immediately after plasma oxidation, the protecting layer of nail polish was peeled from the threaded faces, and the bolts were placed in a Morton flask containing approximately 300 μL of a 1:2 mixture of photocurable hydrophobic liquid (96:2:2 w/w/w dodecyl methacrylate/benzoin isobutyl ether/1,6-hexanediol diacrylate) and ethanol. The container was filled with an approximately isodense aqueous solution of KBr. The hydrophobic liquid precipitated onto the hydrophobic threads of the helical components. Rotation of the container using the motor of a rotary evaporator (rate of rotation ∼30 rpm) caused the components to collide. Fusion of the drops of hydrophobic liquid drove the self-assembly of the components into aggregates. After the self-assembly was complete and rotation stopped, exposure of the aggregates to UV light (100 W, mercury lamp) for 1 h hardened the hydrophobic liquid and generated mechanically stable structures.

We performed each self-assembly experiment three−five times. In all cases we obtained topologically identical structures, even though the number of components included in the aggregates varied by 5−10%.