Spontaneous resolution of silver double helicates consisting of achiral ligands with several aromatic rings†

Qiaozhen Sun, Yan Bai, Guangjie He, Chunying Duan,* Zhihua Lin and Qingjin Meng*

Symmetric breaking of silver double helicates through spontaneous crystallization was achieved *via* incorporation of C–H···π and π–π stacking interactions of achiral ligands consisting of several aromatic rings.

The manipulation of chirality has received a great deal of attention because it plays a pivotal role in the life sciences and materials science. Chirality is expressible at every level of the structures of biological systems and can emerge cooperatively on the molecular scale in chiral supramolecular assemblies.[1] While a large number of chiral superstructures were adopted through covalent arrangements of the chiral building blocks at the molecular level by using the "*bottom-up*" strategy,[2,3] few of the chiral molecules could be resolved spontaneously from the controlled chiral architectures at the supramolecular level, due to the fact that conglomerate formation is not very frequent and is even less predictable in ordered systems.[4,5] As a continuance of our research work on chiral recognition of helical compounds,[6] we focused our interest on spontaneous resolution of chiral helicates by using achiral ligands. Here we realized chiral spontaneous resolution of silver helicates $Ag_2L_2^{2+}$ from achiral ligands, L^1 N',N'-bis[1-(imidazol-4-yl)methylidene]benzil dihydrazone and L^2 N',N'-bis[1-(pyridin-2-yl)methylidene]benzil dihydrazone, respectively (Scheme 1).[7] The atropisomer chiral bridging mode of the ligands translates the chirality of the first metal center to the second one, resulting in the formation of the chiral helicate, and the intermolecular C–H···π and π–π stacking interactions are expected to be homochiral and strong enough to control the chiral aggregation, from which conglomerates are formed and spontaneous resolution on crystallization is achieved.

Reaction of ligand L^1 with $AgNO_3$ generated a silver helicate $Ag_2L^1_2\cdot2NO_3\cdot CH_3OH$ **1**, in high yield (see ESI). Single crystal structure analysis‡ of one crystal exhibits the crystallization of a space group $P3_221$ and the presence of only P helicate. The helical cation has a crystallographic 2-fold axial symmetry; a silver atom is coordinated to two imine and two imidazole nitrogen atoms forming a distorted tetrahedral geometry (Fig. 1). A ligand spans both of the silver ions and transmits the Δ chirality from one silver center to the other. The two silver centers, being of the same chirality, are coordinated by two coupled ligands with Ag···Ag separation of 4.21 Å, leading to the replication of the conformational chirality of the first ligand to the second. The neighboring double helical units are connected together through C–H···π interactions of a carbon atom of an imidazole ring. One of the benzene rings forms a one-dimensional helical 3_2 screw along the c direction with the H···M separation being 2.78 Å and the C–H···M angle being 149° (M is the center of the benzene ring).
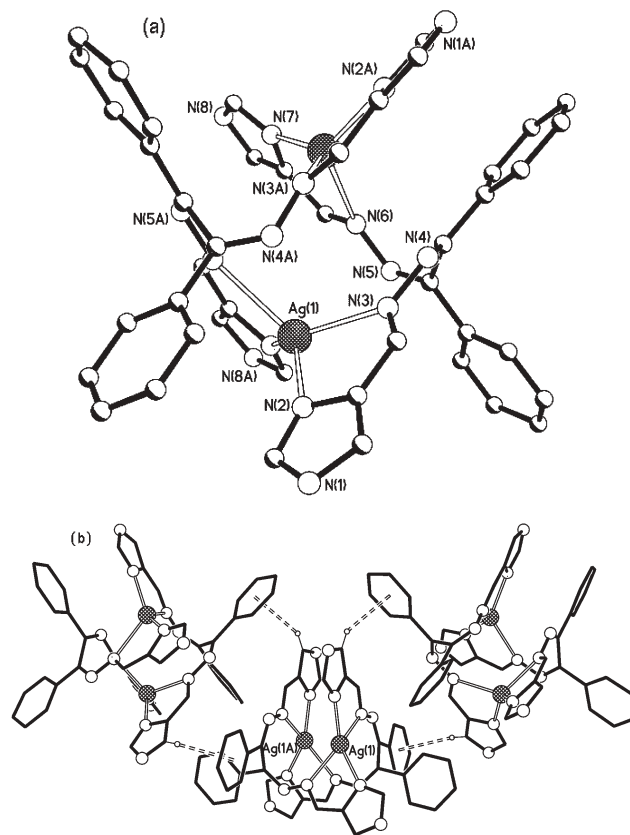

Fig. 1 View of the P conformation of the helicate $[Ag_2L^1_2]^{2+}$ (a) and the chiral 3_2 screw along the c direction through C–H···π interactions (b); H atoms and anions are omitted for clarity. Symmetry code: A: −x, x + y, 1.3333 − z; B: x − y, −y, 1.6667 − z.

Scheme 1

Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing, 210093, P. R. China. E-mail: duancy@nju.edu.cn

Adjacent screws align themselves in parallel and this maintains the *P* helical chirality, featuring a homochiral 3D structure, which is further stabilized through H-bonding between the N–H groups of the imidazole rings and the disordered anions.

Structure analysis of another crystal obtained from the same crystallization reveals that the molecules of **1** also have the potential to crystallize in a space group of $P3_121$, the opposite handedness space group of $P3_221$. The helicates in the latter crystal exhibit the *M* configuration (see ESI), indicating that the formation of conglomerates and the spontaneous resolution of the enantiomers occur during the course of the crystallization. Chiral discriminative interactions have been reported to arise from some substantially strong, selective and directional interactions, such as metal coordination and hydrogen bonding,[8] or even through van der Waals interactions, halogen···π interactions,[9] while the resolution of enantiomeric assemblies through weak C–H···π interactions still remains challenging, due to the lower stability and significantly higher susceptibility to racemization.[10]

To further investigate the absolute configurations of the two enantiomers, solid-state CD spectra of large crystals prepared in the same crystallization were measured. As shown in Fig. 2, the preliminary result demonstrates the formation of either *P* or *M* enantiomers in a crystal, which confirms the spontaneous resolution during the course of crystallization. However, based on the CD measurement of 20 crystals from one crystallization, the enantiomeric excess *ee* ($ee = 100 \times (M - P)/(P + M)$) value for the crystallization is calculated to be about zero, indicating the racemization of the whole crystallization.

Reaction of ligand L^2 with $AgNO_3$ in the presence of excess $NaClO_4$ afforded silver helical compound $Ag_2L^2_2 \cdot 2ClO_4$ **2**. Single crystal structure analysis‡ of one of the crystals exhibits the crystallization of chiral space group $P3_221$ and the presence of only *P* helicate (Fig. 3). The atropisomer chiral bridging mode of the ligands translates the *Δ* chirality of the first metal center to the second one, resulting in the formation of the chiral helicate. The two silver centers, being of the same chirality, are coordinated by two coupled ligands with Ag···Ag separation of 3.74 Å, leading to the replication of the conformational chirality of the first ligand to the second. The π–π stacking interactions between the benzene ring III and the pyridine ring IVA from the symmetry related part of the helicate (symmetry code A: y, x, −z) are found to stabilize the helical mode with the dihedral angle of the stacked pair being 4° and the shortest atom···atom separation being 3.45 Å.
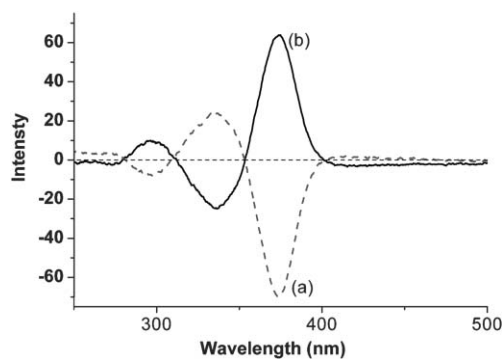

Fig. 2 Solid-state CD spectra of large crystals (0.4 × 0.4 × 0.3 mm) consisting of *P* helicates (a) and *M* helicates (b) showing the contrasting Cotton effects.
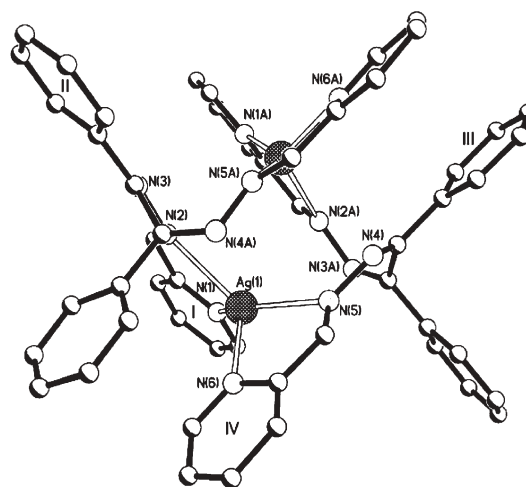

Fig. 3 View of the *P* conformation of the helicate $[Ag_2L^2_2]^{2+}$. Hydrogen atoms are omitted for clarity. Symmetry code A: y, x, −z.

The most interesting structural feature of the crystal packing is that the pyridine IV and benzene IIIB rings from the symmetric related helicate (symmetry code B: −x, −x + y, −⅓ − z) are connected together through face-to-face stacking interactions to form an infinite chain around a 3_2 screw axis (Fig. 4). The shortest inter-planar atom···atom separation is *ca.* 3.55 Å with the dihedral angle of the stacking pair being 18.4°. Meanwhile pyridine IV and benzene rings IIIB interact with other benzene rings II and IIB of the neighbor's through C–H···π interactions. The separations between the hydrogen atoms and centers of the benzene rings (M) are 2.55–2.60 Å with the C–H···M angles being 165–170°.

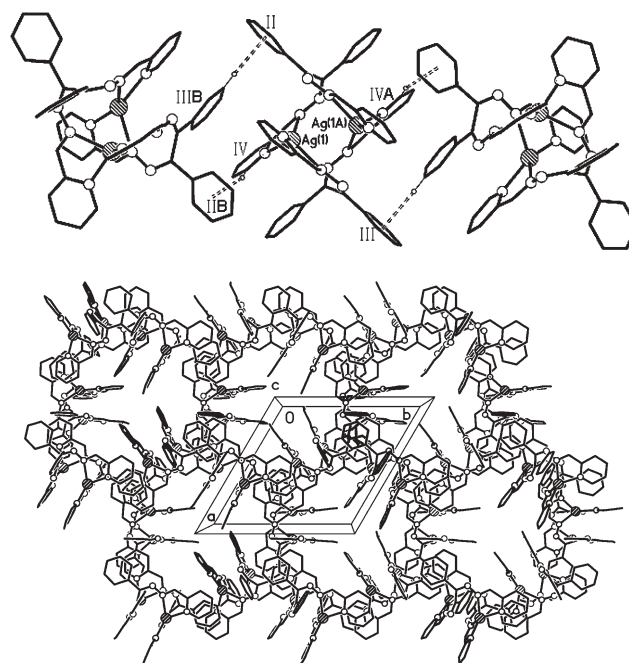**Fig. 4** View of the homochiral π–π stacking interaction cooperating with the C–H···π interactions in a 3_2 infinite helical chain for compound **2** with *P* helicate (top) and the 3D network stabilized by the homochiral interactions (bottom). Symmetry code: A: y, x, 1 − z; B: x − y, 1 − y, ⅔ − z).
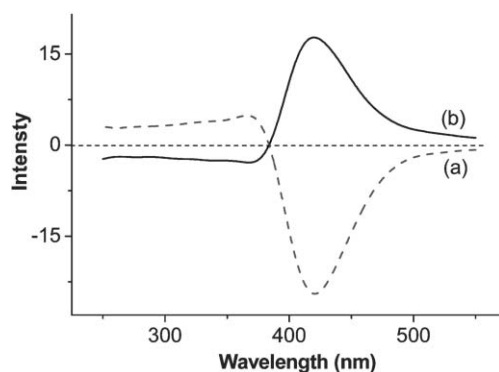
Fig. 5 Solid state CD spectra exhibit the significant Cotton effect of the crystals of compound **2** consisting of *P* (a) and *M* (b) configurations of helicates.

It is obligatory that all metal ions in a 3_2 helical chain have the same *P* chiralities. Since the pyridine and benzene rings located on another part of the helicate also connect their neighbors to form another infinite helical chain along the *c*-axis, a three-dimensional (3D) chiral network in which all the double helices and all the silver atoms have the same chiralities should be achieved. The structural simplicity of the building blocks and the ability to control the assembly process by means of conformational chiral centers make this system promising for the development of a wide range of homochiral supramolecular materials. In fact the adoption of a chiral space group by the compound prompted an investigation of the optical activity with SHG (Second Harmonic Generation) response about 5 times that of KDP (KH_2PO_4).

While the solution didn't exhibit any CD signal, the preliminary investigation in the solid state showed a negative Cotton effect (Fig. 5), indicating the formation of excess *P* enantiomer.[2] Detailed CD measurements on about 20 crystals from one crystallization (hexagonal prism with the length of *ca*. 0.50 mm and height of *ca*. 0.30 mm) suggest that the enantiomeric excess *ee* is 60%. The structure of a crystal exhibiting a positive Cotton effect (see ESI) shows the existence of *M* helicates and the crystallization of a $P3_121$ space group with the homochiral three-dimensional network consisting of *M* molecules.

Generally, the occurrence of bulk crystal chirality should be described as a chiral autocatalytic spontaneous symmetry breaking in which the secondary nucleation is cloned by the parent crystal: *the crystal nuclei in the vicinity of an existing "parent" crystal have the same crystal structure as the parent crystal*.[11] It is suggested that the presence of two silver atoms and two ligands may lead to a cooperative effect whereby the homochiral entity precipitates. Since all the components are achiral, the induced chirality must arise from a spontaneous process. Another important factor in the symmetric breaking is the statistical nature of the spontaneous crystallization. From the investigation of crystals in 50 independent crystallizations (20 crystals picked up from one crystallization were measured for each independent crystallization), we found that the intensities generated a bimodal probability distribution (see ESI), like that observed in the 1,1′-binaphthyl melt and the crystallization of $NaClO_3$.[12]

This work was supported by the National Science Foundation of China.

1 R. Oda, I. Huc, M. Schmutz, S. J. Candau and F. C. MacKintosh, *Nature*, 1999, **399**, 566–569; E. Yashima, K. Maeda and Y. Okamoto, *Nature*, 1999, **399**, 449–451; J. M. Ribó, J. Crusats, F. Sagués, J. Claret and R. Rubires, *Science*, 2001, **292**, 2063–2066.
2 L. J. Prins, J. Huskens, F. D. Jong, P. Timmerman and D. N. Reinhoudt, *Nature*, 1999, **398**, 498–502.
3 L. J. Prins, F. D. Jong, P. Timmerman and D. N. Reinhoudt, *Nature*, 2000, **408**, 181–184; J. H. K. K. Hirschberg, L. Brunsveld, A. Ramzi, J. A. J. M. Vekemans, R. P. Sijbesma and E. W. Meijer, *Nature*, 2000, **407**, 167–170.
4 L. Pérez-García and D. B. Amabilino, *Chem. Soc. Rev.*, 2002, **31**, 342–356; J. Jacques, A. Collet and S. H. Wilen, *Enantiomers, Racemates and Resolutions*, Krieger Publishing Company, Malabar, Florida, 1994.
5 L. Addadi and M. Lahav, *Origin of Optical Activity in Nature*, Ed.: D. C. Walker, Elsevier, New York, 1979, chap. 14; S. E. Mason, *Nature*, 1984, **311**, 19–23; J. Chela-Flores, *Chirality*, 1991, **3**, 389–392.
6 C. J. Fang, C. Y. Duan, D. Guo, C. He, Q. J. Meng, Z. M. Wang and C. H. Yan, *Chem. Commun.*, 2001, 2540–2541; C. J. Fang, C. Y. Duan, C. He and Q. J. Meng, *Chem. Commun.*, 2000, 1187–1188; Y. Bai, C. Y. Duan, P. Cai, D. B. Dang and Q. J. Meng, *Dalton Trans.*, 2005, 2678–2680.
7 P. K. Pal, S. Chowdhury, M. G. B. Drew and D. Datta, *New J. Chem.*, 2000, **24**, 931–933; S. Chowdhury, P. B. Iveson, M. G. B. Drew, D. A. Tocher and D. Datta, *New J. Chem.*, 2003, **27**, 193–196; S. Chowdhury, M. G. B. Drew and D. Datta, *New J. Chem.*, 2003, **27**, 831–835.
8 I. Katsuki, Y. Motoda, Y. Sunatsuki, N. Matsumoto, T. Nakashima and M. Kojima, *J. Am. Chem. Soc.*, 2002, **124**, 629–640; E. Q. Gao, Y. F. Yue, S. Q. Bai, Z. He and C. H. Yan, *J. Am. Chem. Soc.*, 2004, **126**, 1419–1429; U. Knof and A. von Zelewaky, *Angew. Chem., Int. Ed.*, 1999, **38**, 302–322; Y. V. Mironov, N. G. Naumov, K. A. Brylev, O. A. Efremova, V. E. Fedorov and K. Hegetschweiler, *Angew. Chem., Int. Ed.*, 2004, **43**, 1297–1300; A. Orita, T. Nakano, D. L. An, K. Tanikawa, K. Wakamatsu and J. Otera, *J. Am. Chem. Soc.*, 2004, **126**, 10389–10396; T. Giorgi, S. Lena, P. Mariani, M. A. Cremonini, S. Masiero, S. Pieraccini, J. P. Rabe, P. Samori, G. P. Spada and G. Gottarelli, *J. Am. Chem. Soc.*, 2003, **125**, 14741–14749.
9 M. Lahav and L. Leiserowitz, *Angew. Chem., Int. Ed.*, 1999, **38**, 2533–2536; R. K. R. Jetti, A. Nangia, F. Xue and T. C. W. Mak, *Chem. Commun.*, 2001, 919–920.
10 J. W. Steed and J. L. Atwood, *Supramolecular Chemistry: An Introduction*; J. Wiley & Sons: Chichester, 2000; G. R. Desiraju and T. Steiner, *The Weak Hydrogen Bond*; OUP/IUPAC: Oxford, 1999.
11 D. K. Kondepudi and K. Asakura, *Acc. Chem. Res.*, 2001, **34**, 946–954; K. Mikami and M. Yamanka, *Chem. Rev.*, 2003, **103**, 3369–3400; R. Plasson, H. Bersini and A. Commeyras, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 16733–16738.
12 D. K. Kondepudi, J. Laudadio and K. Asakura, *J. Am. Chem. Soc.*, 1999, **121**, 1448–1451; D. K. Kondepudi, R. J. Kaufman and N. Singh, *Science*, 1990, **250**, 975–977.