Hierarchically ordered chiral crystals have attracted intense research efforts for their huge potential in optical devices, asymmetric catalysis and pharmaceutical crystal engineering. Major barriers to the application have been the use of costly enantiomerically pure building blocks and the difficulty in precise control of chirality transfer from molecular to macroscopic level. Herein, we describe a strategy that offers not only the preferred formation of one enantiomorph from racemic solution but also the subsequent enantiomer-specific oriented attachment of this enantiomorph by balancing stereoselective and non-stereoselective interactions. It is demonstrated by on-demand switching the sign of fan-shaped crystal aggregates and the configuration of their components only by changing the molar mass of tailored polymeric additives. Owing to the simplicity and wide scope of application, this methodology opens an immediate opportunity for facile and efficient fabrication of one-handed macroscopic aggregates of homochiral organic crystals from racemic starting materials.

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Hierarchically ordered chiral assemblies like biominerals, scales, plant fibers are abundant in nature and play indispensable roles in the whole process of life. They have inspired the development of artificial systems showing huge potential in chiral resolution, asymmetric catalysis, optical devices, chiral sensors, pharmaceutical crystal engineering, and so forth. The formation of these chiral biostructures relies on the accurate recognition and screening of optically active compounds as well as the precise hierarchical self-assembly of building blocks that are selected. Even though unnatural chiral compounds (e.g., α-amino acids and saccharides) are accidently ingested by taking artificial foods and medicines, they would hardly be incorporated into biomolecules and the corresponding assemblies. In contrast, to form optically active structures, man-made strategies currently available have to either use enantiomerically pure components or separate the mixture of assemblies with mirror-images formed from racemic compounds through a self-sorting process, due to lacking the ability of auto-screening unfitted building blocks. Stereoselective generation of hierarchically ordered chiral crystals of a single enantiomer from a racemic solution in one-step would greatly improve the production efficacy but has never been realized.

Oriented attachment (OA) is an efficient method to generate hierarchically ordered crystals which is a dynamically preferential pathway to reduce surface energy of small particles by ordered attaching solid phase blocks to the growing surfaces, especially in high concentration solutions. Stabilized crystalline building blocks with high shape anisotropy are essential to this process, which can be achieved by using additives or particular ripening conditions. Rac-threonine has been reported to form the mixture of right- and left-handed crystal clusters through enantiomer-specific oriented attachment (ESOA), and only 85% ee can be achieved for each of them. By using chiral additives, imperfect OA occurs and chiral mesocrystals can be generated. For examples, small chiral molecules are often used as additives to fabricate chiral mesocrystals by being incorporated between two crystalline plates and inducing twisted alignment of these subunits. Most of the building blocks are inorganic materials, studies on pure organic chiral mesocrystals are rarely reported. The attempt to obtain chiral meso-structure from rac-alanine has been conducted by using chiral double-hydrophilic block copolymers. It was found that although no chiral resolution was achieved, the polymeric additives could stabilize the crystalline subunits and thus changed the crystal habit. The additives selectively attach on the specific crystal faces and slow down their growth. This rule has long been applied for stereoselective crystallization of conglomerates. Chiral additives delay the nucleation and growth of one enantiomorph with the same configuration through stereoselective adsorption. In fact, the attachment of the additives with opposite configuration can also change the morphology of the crystal owing to the non-stereospecific interactions between the additive molecules and specific faces. However, the non-stereoselective interactions have been overlooked in building hierarchically ordered chiral organic crystals. We posit that macroscopic homochiral crystal aggregates of a single enantiomer could be generated from a racemic solution by virtue of synergistic combination of stereoselective and non-stereoselective interactions.

Herein, we describe a strategy that enables the preferred formation of one enantiomorph directly from racemic solutions as well as their in-situ OA to fabricate macroscopic chiral crystal aggregates.
aggregates, only aided by the tailored polymeric additives with various molar masses. When a L-polymer with a medium molar mass is used, Plus (P)-type fan-shaped crystal aggregates of D-p-hydroxyphenylglycine p-toluenesulfonate (D-pHpgTs) are obtained (Fig. 2a). Changing the molar mass of the polymer can switch the chirality of the hierarchically ordered structures thus formed on both molecular and supramolecular levels (Supplementary Fig. 1).

Results

Formation of homochiral crystal aggregates. Nine narrowly distributed poly[p-methacrylamido tert-butoxycarbonyl-L-phenylalanine] (L-PMPABoc)s with number-average molar masses ($M_n$) ranging from 5700 to 30,100 Da were synthesized by reversible addition-fragmentation chain transfer radical polymerization, followed by purification using preparative gel permeation chromatography. The corresponding deprotected poly[p-methacrylamido-L-phenylalanine]s (L-PMPAs) were named as P1–P9 (Table S1, Supplementary Fig. 2). The polymer with a moderate molar mass, i.e. P5 ($M_n = 13,500$ Da, PDI = 1.10), was first used as the additive to verify our ideas. rac-pHpgTs was chosen as a model substrate. Into a supersaturated solution of rac-pHpgTs (2.5 g of rac-pHpgTs in 10 mL of 0.5 M p-toluenesulfonic acid aqueous solution), that was prepared and filtrated at 60 °C, 1.5 wt% (polymer/rac-pHpgTs) of P5 was added. The crystallization was allowed to take place at 25 °C. After a period of time, the formed crystals were collected by filtration and washed with cold acetone. After drying under vacuum, their morphologies were examined by optical and electron microscopes (Supplementary Methods).

Fan-shaped crystal aggregates were exclusive species when P5 was used as the additive (Fig. 2b), which was quite different from randomly distributed needle-like crystals formed in the absence of additive (Fig. 2f, Supplementary Fig. 4). The height map of fan-shaped crystals given by optical microscope with a large depth-of-field (Fig. 2c, inserted picture) displayed a gradually rising profile from the right edge to the left edge, indicating a macroscopic P-type twisting sense which is just like a left-handed folding fan (Fig. 2d). Occasionally, crystals with two-blade propeller morphology were observed (Fig. 2e), where the twisting sense...
was more obvious. Further investigation showed that the fan-shaped structures were composed of small platelets (Supplementary Fig. 5). Chiral HPLC tests showed that the P-type fan-shaped crystals consisted of D-pHpgTs exclusively (Supplementary Fig. 6a), while needle-like crystals obtained in blank control experiment were the mixtures of enantiomers consisting of D- and L-pHpgTs, separately (Supplementary Fig. 7). Crystallization was also carried out in optically pure D-pHpgTs solution. Only needle-like crystals were obtained in the absence of additives. Whereas, fan-shaped crystals were produced when P5 was added (Supplementary Fig. 8). These results proved that the emergence of fan-shaped crystals was attributed to the presence of chiral additives but not merely the chirality of amino acid itself.

Crystals obtained at different time were collected and examined by SEM and circular dichroism spectra (CD) to investigate the evolution process. Three distinct stages could be identified in the crystallization process (Fig. 2g–k, Supplementary Fig. 9). In the first 10 min (stage I), small round particles were dominated, although some tiny crystals with a length around 1 μm could also be found occasionally (Fig. 2g). The CD signal grows linearly until it reaches a plateau (Supplementary Fig. 10a, b). From 30 min to 5 h (stage II), more tiny crystalline platelets appeared. Meanwhile, the stacking of two or three platelets at a twisting angle of $-1 \sim -2^\circ$ (counterclockwise) was also present (Fig. 2h, i) with the CD signal increasing further (Supplementary Fig. 10b). During this period, the crystals grew up to a length of 40 μm and the prototype of fan-shaped crystals began to emerge. From 7 to 13 h (stage III), fan-shaped crystals were observed. These crystals had a length around 600 μm and a width around 160 μm (Fig. 2j, k). Moreover, several steps from the right edge to left edge were observed (Fig. 2k and Supplementary Fig. 11). At this time, a well-developed cotton effect appears in CD spectrum, indicating the emergence of high-level chirality (Supplementary Fig. 10c). These results suggested that the final fan-shaped crystals were gradually assembled by the platelet sub-structures that formed in the earlier stages through imperfect OA process.

To further confirm this assumption, the self-assembling of pre-prepared D-pHpgTs crystals was conducted. Needle-like D-crystals were prepared by recrystallization of D-pHpgTs without adding any additive and grow lightly to smaller sizes. They were then added into the saturated solution of D-pHpgTs at room temperature followed by adding 1.5 wt% P5. After a period of ripening, crystals were filtrated out and observed by SEM. Morphological reconstruction was examined (Supplementary Fig. 12): in the first 4 h, the surfaces of needle-like crystals were partially dissolved and the crystal edge became blurred. From 4 h to 24 h, platelets with new developed faces and aggregates of two or three platelets were observed. Ordered arranged crystal aggregates formed after 108 h.

**Chirality tuning.** The twisting sense of the fan-shaped crystal aggregates and the configuration of constituting amino acid molecules were highly dependent on the $M_s$ of the polymeric additives at a fixed concentration of 1.5 wt% (Fig. 3a). Although P5 yielded exclusively P-type fan-shaped crystal aggregates consisting of D-pHpgTs, predominant Minus (M)-type fan-shaped crystal aggregates consisting of L-pHpgTs along with some needle-like crystals consisting of D,a,a were obtained when $p$-methacrylamido tert-butoxycarbonyl-L-phenylalanine (L-monomer) or L-PMPAs with relative low $M_s$ (i.e. P1–P3) were used (Fig. 3d, Supplementary Figs. 13–16). The formation of M-type fan-shaped crystals showed a similar but faster evolution process (Supplementary Fig. 17). And the neighboring platelets twisted around $1 \sim 2^\circ$ (clockwise, Fig. 6b). In the case that L-PMPAs with larger $M_s$ (P8–P9) were used, roughly equal amount of M- and P-type fan-shaped crystal aggregates were obtained (Fig. 3d). Moreover, CD spectra of M- and P-type crystals showed opposite cotton effect at the absorption range which is consistent with the HPLC results (Supplementary Fig. 18).

The chirality bias and morphologies of the crystal aggregates were also dependent on the additive concentration. Although 1.5 wt% of L-monomer resulted in M-type fan-shaped aggregates of L-pHpgTs crystals, raising the amount of L-monomer to 10 wt% switched the twisting sense of crystal aggregates and the configuration of constituting amino acid (Fig. 3b). Besides, increasing the amount of P9 (up to 5.0 wt%) raised the ee% value of the resultant crystals (Fig. 3c) and P-type fan-shaped crystals became the dominated products. Overall, the macroscopic and molecular chirality can be tuned at the same time by changing the molar masses of polymeric additives (Supplementary Table 2), which has never been reported in the formation of hierarchically ordered crystals. In traditional methods, chirality tuning of hierarchical structures is usually achieved by changing the chirality of chiral component.\(^{19–21,25}\) It is also reported that the apparent chirality can be switched by extending aging time\(^{22,42}\) as the building blocks have a staggered orientation that leads to an overall helical structure in one handedness, while the complex aggregates formed by these structures show helicity in the other handedness.

**Distribution of polymeric additives.** The distribution of the polymers in crystals was investigated. Fluorescein labeled polymer (L-PMPA(Flu)) with a similar $M_s$ as P5 was prepared (see Supplementary Method and supplementary Table 1)\(^{43}\). And the crystallization was carried out under the same condition mentioned above. The crystals were collected to test their emission. The contents of polymers in the crystals were calculated to be 0.2 wt% according to the standard curve (Fig. 4a and Supplementary Fig. 19), indicating a high purity of crystals. Furthermore, the fluorescent images showed that the small amount of polymers selectively gathered on the long-axis direction of each single crystalline unit (Fig. 4b, c). To investigate whether the polymers exist between two crystalline building blocks, two models were discussed. If polymers existed between two neighboring platelets, the fluorescent image of the cross-section in x direction should be a periodic pattern of light and shade, and the cross-section in y direction should have a similar periodic fluorescent image (Supplementary Fig. 20). If polymers weren’t involved between two platelets, the fluorescent image of the cross-section in x or y direction should be a step-like pattern (Fig. 4e). Actually, in our case, no periodic fluorescent spots along the z axis in 3D fluorescent images (Fig. 4d), indicating there is no polymer-crystal-polymer sandwich structures. Besides, the fluorescent spots on the x-z plane gradually rose from $+z$ to $-x$ and the fluorescent spots on the y-z plane gradually rose from $+y$ to $-y$ (yellow arrows in Fig. 4d), which was consistent with the step-like fluorescent pattern shown in Fig. 4e. When the crystals were progressively dissolved by cold water, the intensity of fluorescence emission dropped dramatically (Supplementary Fig. 21), indicating again that the polymers only existed on the surface of the whole crystal and no polymer existed between two subunits.

Double-hydrophilic block copolymers has been reported to act as a glue to adhere tightly to the polar faces and join the tiny crystals together. However, in our case, the side-chains of the polymer are hydrophilic and the mainchain is hydrophobic. When the side chains attached onto the polar face of one crystal platelet, the outside mainchains could not attach onto another one to join them together. Besides, due to the relatively weak non-

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stereospecific interactions, it is highly possible for these polymers to leave through adsorption-desorption dynamic processes. When the OA happened, the polymers desorbed from the adhering area to reduce surface energy and resided only on the exposed surface.

Computational simulations. To investigate how the polymers influence the crystal habit, computational simulations were conducted. Single-crystal of $D$-$p$HpgTs belongs to orthorhombic system ($a = 5.45$ Å, $b = 14.41$ Å, $c = 19.57$ Å) with $P2_12_1$ symmetry (Fig. 5a and Supplementary Fig. 22c, d). The crystal habit was observed by SEM and simulated by corrected attachment energy (AE) model based on the unit cell (Supplementary Theory). The crystal habit in pure water was predicted to be a rod-like prism and elongated along the a direction (Fig. 5b), which was identical to the actual single-crystal (Fig 5a). The {0 1 1}, {0 0 2}, {1 0 1} and {1 1 0} faces were exposed, and their surface chemistry and topography could be revealed (Supplementary Fig. 23): {0 1 1} faces were the most polar faces, which were along the polar b axis and topography could be revealed (Supplementary Fig. 23). {0 1 1} and {1 0 1} faces were exposed, and their surface chemistry and their inner and apparent chirality can be tuned by changing additives’ molar masses: (i-vi) Optical micrographs of the crystals obtained by using polymers with different $M_n$s (8000, 13500 and 30100 Da) as additives. (i-vi) the corresponding partially enlarged SEM images, showing the detailed morphologies of the fan-shaped crystals. Scale bar: 200 μm.

Fig. 3 Chirality tuning by using polymeric additives with various molar masses. a The ee% values of the obtained crystals by using L-monomer or L-polymers with various molar masses as additives. Error bars are standard errors calculated from five independent experiments. b The ee% values of the obtained crystals by using different amount of P9. c The ee% values of the obtained crystals by using different amount of L-monomers. d The ee% values of the obtained crystals by using different amount of P9. e The hierarchically ordered crystals were generated from racemic solutions and their inner and apparent chirality can be tuned by changing additives’ molar masses: (i-vi) Optical micrographs of the crystals obtained by using polymers with different $M_n$s (8000, 13500 and 30100 Da) as additives. (i-vi) the corresponding partially enlarged SEM images, showing the detailed morphologies of the fan-shaped crystals. Scale bar: 200 μm.
It turned out that the lowest total energy for \( D/L \) well as the formation of hierarchically ordered chiral crystal (Supplementary Fig. 34). The {1 0 1} faces also showed high polarity, but the facet area was much smaller than that of {0 1 1} faces, making it unlikely to attach from this direction.

\( L \)-monomer and short chain \( L \)-PMPA interact stereoselectively with the clusters of \( L \)-pHgpgTs. However, the strength is weak and cannot inhibit the crystallization of this enantiomer due to the low molar masses of additives. Whereas, the fast adsorption-desorption equilibrium on {0 1 1} and {1 0 1} faces change the crystal habit of \( L \)-pHgpgTs and favor the OA process. Also due to the weak non-stereoselective interactions exerted by \( L \)-monomer and short chain \( L \)-PMPA, the crystal nucleation and growth of \( D \)-pHgpgTs are not obviously affected, and needle-like crystals are obtained. When long chain \( L \)-PMPA were used, the strong non-stereoselective interactions with \( D \)-pHgpgTs change its crystal habit and induce P-type

Mechanisms. On the basis of these results, it is possible to elucidate the interactions between the additives and the crystals as well as the formation of hierarchically ordered chiral crystal aggregates. \( D/L \)-pHgpgTs forms polar crystals and displays well-developed \{0 1 1\} faces, where -NH\(_3\)\(^+\), -COOH and -SO\(_3\)\(^-\) groups face straight outward, and \{1 0 1\} faces along a axis where -COOH and -SO\(_3\)\(^-\) groups exposed. \( L \)-PMPA with phenylalanine side groups can attach on these polar faces by multiple hydrogen bonds, and the relative strength depends on molar masses of additives at a fixed concentration\(^{44-46}\)

\( L \)-PMPA with an optimized chain length (i.e., P5) interacts stereoselectively and strongly with the clusters of the solute molecules with same configuration (i.e., \( L \)-pHgpgTs), that are smaller than the critical nucleus size, and efficiently inhibits the crystal nucleation and growth. In the meantime the \( L \)-PMPA molecules can also bind on the specific surfaces of \( D \)-pHgpgTs crystals through non-stereoselective interactions. Although such interactions are relatively weak and cannot stop the crystallization of \( D \)-pHgpgTs, the crystal growth perpendicular to \{0 1 1\} and \{1 0 1\} faces is delayed. With the enlarged area of these faces, the \( D \)-pHgpgTs crystals are oriented along the a direction and stacked together along the b direction to reducing their high surface energy (Supplementary Fig. 28). Powder XRD showed that the intensity of (0 1 1) peak was increased and that of (0 0 2) peak was decreased when 1.5 wt% of P5 was used as the additive (Supplementary Fig. 33). The \{1 0 1\} faces also showed high polarity, but the facet area was much smaller than that of \{0 1 1\} faces, making it unlikely to attach from this direction.

In order to study the relationship between molecular chirality and macroscopic chirality of fan-shaped crystals, the attachment angle of two morphological changed \( D \) or \( L \)-pHgpgTs crystals were calculated by building a model box containing a main crystal and a smaller one. The two crystalline layers were attached by (0 1 1) and (0 -1 -1) faces, and the total energy was calculated when the upper layer was rotated from -6\(^\circ\) to +6\(^\circ\) (Supplementary Fig. 34). It turned out that the lowest total energy for \( D \)-crystals appears at -1\(^\circ\) (Supplementary Fig. 35a), while the lowest total energy for \( L \)-crystals appears at +1\(^\circ\) (Supplementary Fig. 35b), which showed a good agreement with the experimental results. As the electrostatic interaction is dominant in the total energy (Supplementary Fig. 35c), the possible reason may be that the ion pairs on the interface can be perfectly matched only when the two layers rotate a small angle.

**Fig. 4** The residual amount of \( L \)-PMPA(\( Flu \)) and their distribution in the crystal aggregates of \( D \)-pHgpgTs. a Fluorescence emission spectrum of \( L \)-PMPA(\( Flu \)) aqueous solutions with different concentration (0.0025-0.1 mg/mL), the dashed line is the curve of crystal sample (100 mg crystals dissolved in 10 mL H\(_2\)O). b Merged picture of optical micrograph and fluorescence image of fan-shaped crystal aggregates of \( D \)-pHgpgTs when 1.5 wt% \( L \)-PMPA(\( Flu \)) was used as the additive. e The corresponding 2D confocal fluorescence micrographs. d The 3D confocal fluorescence profile of one fan-shaped \( D \)-crystal. e The model for the situation that no polymers exist between two crystalline platelets but only on the surface of the whole fan-shaped crystal, and the corresponding fluorescein patterns on the cross-sections (blue plane: cross-section in y direction; red plane: cross-section in x direction). The crystal habit was simplified to a rectangular block for better classification. The molecular structure of \( L \)-PMPA(\( Flu \)) is illustrated on the left.
fan-shaped crystal aggregates. On the other hand, the stereoselective interactions with L-pHpgTs cause uneven local concentration of the additives. The crystal nucleation and growth of this enantiomer are not inhibited, but the crystal habit is changed. As a result, either M- or P-type fan-shaped crystals composed of L- and D-pHpgTs, respectively, are obtained.

Raising the concentrations of additives helps the adsorption on L-clusters through stereoselective interactions and the crystals of D-pHpgTs through non-stereoselective interactions. The crystallization of L-pHpgTs is thus inhibited while P-type fan-shaped crystal aggregates of D-pHpgTs are obtained.

**Applicability.** To explore the scope of this method, the crystallizations of racemic threonine (rac-Thr), allothreonine (rac-aThr), aspartic acid (rac-Asp) and aspartic acid copper complex (rac-Asp$_2$Cu) were carried out in the presence of Poly(N-methacryloyl-L-lysine) (L-PMAL). In all cases, D-crystals with over 90 ee% were obtained. More importantly, crystal aggregates were always observed when L-PMAL was used as additive. Specifically, D-Asp$_2$Cu crystals (92.3 ee%) with P-type helical morphology were generated in 6 h when 5 wt% L-PMAL ($M_m = 7500$ Da) was added, whereas only disordered granular crystals were obtained, whereas only disordered granular crystals were observed in blank control (Fig. 6d–f).

**Discussion.** We have reported a strategy to prepare chiral crystal aggregates of a single enantiomer from a racemic solution by using tailored polymeric additives. The chirality on both molecular and macroscopic levels can be switched by changing the molar masses of additives. Particularly, P-type fan-shaped crystal aggregates of D-pHpgTs are obtained when L-PMAL with an optimized molar mass is used. This unique and efficient chiral regulation method is realized by balancing the strength of stereoselective and non-stereoselective interactions between L-additive and D/L-pHpgTs.
nucleus and crystals. The application of this method has successfully been extended to other conglomerate forming racemates (i.e. Thr, aThr, Asp, and AspCu) by using L-PMAL as the additive. It has considerably simplified the fabrication protocol of hierarchical chiral structures from racemic compounds. Low additive dosage and high purity of the crystalline product also make it suitable for large scale production. This work would inspire further research to increase our fundamental understanding in accurate chiral discrimination and cross-scale, multi-level transmission, and expand the scope of accessible building blocks. We envision the potential wide applications of this strategy in pharmaceutical crystal engineering, organic chiral micro-/nano-laser, and asymmetric catalysis.

Data availability
The data that support the findings of this study are available from the corresponding author upon request. The Crystallographic data generated in this study have been successfully been extended to other conglomerate forming racemates (i.e. Thr, aThr, Asp, and AspCu) by using L-PMAL as the additive. It has considerably simplified the fabrication protocol of hierarchical chiral structures from racemic compounds. Low additive dosage and high purity of the crystalline product also make it suitable for large scale production. This work would inspire further research to increase our fundamental understanding in accurate chiral discrimination and cross-scale, multi-level transmission, and expand the scope of accessible building blocks. We envision the potential wide applications of this strategy in pharmaceutical crystal engineering, organic chiral micro-/nano-laser, and asymmetric catalysis.

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Author contributions
X.H.W. supervised the research. X.C.Y. and X.H.W. contributed to the conception, design of experiments, drafting and critical revision of the manuscript; X.C.Y., B.W.L., Z.X.W. and J.L. contributed to synthesis, analysis and data collection; J.Z. contributed to discussion of experiment results and revision of the manuscript.

Competing interests
The authors declare no competing interests.

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