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Fu Huang, Lishuang Ma, Yanke Che, Hua Jiang, Xuebo Chen, and Ying Wang J. Org. Chem., Just Accepted Manuscript • DOI: 10.1021/acs.joc.7b02709 • Publication Date (Web): 27 Dec 2017 Downloaded from http://pubs.acs.org on December 27, 2017

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A Corannulene-based Coordination Cage with Helical Bias

Fu Huang^{†,‡,#}, Lishuang Ma^{†,#}, Yanke Che[‡], Hua Jiang^{*†,§}, Xuebo Chen^{*†}, and Ying Wang^{*†}

[†]Key Laboratory of Theoretical and Computational Photochemistry and Key Laboratory of Radiopharmaceuticals, Ministry of Education; College of Chemistry, Beijing Normal University, Beijing 100875, China

[‡]Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

⁹School of Chemical & Environmental Engineering, Wuyi University, Jiangmen 529020, China

Supporting Information Placeholder

ABSTRACT: We report here the first corannulene-based molecular cage, constructed via metal-induced self-assembly of corannulene-based ligands. In sharp contrast to those assembled via the planar π -conjugated analogues of corannulene, at ambient and elevated temperatures, the molecular cage exists as an ensemble

of four stereoisomers (two pairs of enantiomers), all of which possess a D_5 symmetric (regardless of the counter-anions) and inherently helical structure. Decreasing the temperature shifts the equilibrium between different pairs of enantiomers. At low temperature, only one pair of enantiomers is present. Helical bias for the cage could be efficiently achieved by inducing-asymmetry with enantiopure anions. When non-enantiopure anions are used, the asymmetryinduction abides by the "majority rule", i.e., the major enantiomer of the chiral anions controls the bias of helical sense of the cages.

INTRODUCTION

Synthetic molecular entities having cage-like structures and well-defined inner cavities have received great interest.1 Such molecular cages can act as molecular flasks used in catalysis,² material purification,³ reactive intermediate storages,⁴ and drug delivery.⁵ In particular, chiral cages⁶ could be employed in asymmetric catalysis and enantiomeric resolution. Self-assembly with high-symmetry building blocks containing a concave chemical surface is a general, highly-efficient synthetic strategy that gives rise to molecular cages.⁷ Besides, this is also one of main approaches for constructing chiral cages, in which chirality of the cage arises from curvature of its molecular scaffold.⁸ There are only a few known concave building blocks for cage constructions, with a majority adopting either a conical or subulate geometry.79 As such, new building blocks with smaller curvature that could potentially extend the geometric diversity and applications of such constructed cages are desirable.

Corannulene is a bowl-shaped polycyclic aromatic hydrocarbons that has $C_{5^{\nu}}$ symmetry, with curvature mimicking that of fullerene[60].¹⁰ Due to its special structural geometry, corannulene is endowed with many intriguing properties, such as a curved π -surface, a large dipole moment,¹¹ inherent charity,⁸ intricate redox behavior,¹² and high reactivity^{10b}. More interestingly, corannulene dynamically undergoes a very rapid bowl-to-bowl inversion in solution due to the low inversion barrier (10.2 kcal mol⁻¹



at 209 K),¹³ which provide corannulene a dynamic, switchable molecular chirality. By virtue of some of these properties, especially the high reactivity and the concave curved π -surfaces, a number of corannulene-based molecular entities, including dendrimer,¹⁴ liquid crystal,¹⁵ clefts,¹⁶ and supramolecular polymers,¹⁷ with unique properties or functions, have been constructed for various purposes. Nevertheless, to date, a corannulene-containing molecular cage is, to the best of our knowledge, unprecedented.¹⁸

We envisioned that the distinct characteristics of corannulene would make it an excellent candidate to construct molecular cages with intriguing properties, in particular, the chirality, the conformational diversity, and good impermeability. In this contribution, we report the synthesis, characterization and asymmetric induction of the first corannulene-based coordination molecular cage, $[Ag_51_2]^{5+}$ (Figure 1), as results of our initial investigation on such kind of cage systems.

RESULTS AND DISCUSSION

Design, Synthesis and Characterization. The precursor of the cage, ligand 1, was designed to possess a corannulene skeleton with five pyridine units appended. An *iso*-butoxy side chain was introduced into each pyridine ring at the *meta* position to pyridine-N for better solubility while posing no interference with the ligandmetal coordination. Molecular cages were expected to be formed through the self-assembly of 1 induced by



Figure 1. Structures of corannulene, the corannulene-based ligand **1**, and mixture of four $[Ag_5\mathbf{1}_2] \cdot [OTf]_5$ cage conformers (denoted $[mix-Ag_5\mathbf{1}_2] \cdot [OTf]_5$) studied herein.

Scheme 1. Synthesis of ligand 1.^a

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^{*a*} Reagents and conditions: (i) 1-iodo-2-methylpropane, K_2CO_3 , DMF, 60 °C, 8 h (65%); (ii) bis(pinacolato) diboron, Pd(dppf)₂Cl₂, KOAc, DMSO, 80 °C, 8 h (80%); (iii) ICl, DCM, from -78 °C to rt, 82 h (50%); (iv) Pd(PPh₃)₄, K₃PO₄, benzene/ethanol/water, 100 °C, 6 d (50%).

metal cations favoring linear coordination geometry such as Ag⁺ cations.^{6a,19}

Synthetic routes for ligand 1 was outlined in Scheme 1. Ligand 1 was synthesized in three steps by O-alkylation of 3-bromo-5-hydroxypyridine with alkyl iodide, borylation with bis(pinacolato)diboron, and a Suzuki cross-coupling reaction with 1,3,5,7,9-pentachlorocorannulene. The structure of 1 was confirmed by NMR and high-resolution mass spectra (see the Supporting Information (SI)).

Due to the chirality and the bowl-shape of corannulene, the ligand 1 itself exists as a pair of M/P enantiomers

(Figure S₁);¹⁸ and once complexed, the pyridyl units on each ligand tilt in one of two possible directions, giving rise to a left- or right-handed propeller-shaped geometry (*M* or *P* helicity). However, considering the geometric restraints imposed by the Ag⁺ linear coordination, only two pair of enantiomers of $[Ag_{5}I_{2}]^{5+}$, P,M,P and M,P,M, and P,P,P and M,M,M, can be expected (Figure 1), in which the designations of the chirality of substituted corannulene are based on the general rules for molecular entities possessing axial chirality, such as foldamers, but with the additional rule that the bowl-shape corannulene opens up (Figure S1 and S2, SI). Nevertheless, this will be still in sharp contrast to that of traditional Ag_xL₂-type cages,^{6a,19a, 20} for which there is only one steady structure or one pair of enantiomers presented in the systems. Given the dynamic molecular chirality of the corannulene moiety, interconversion between the enantiomeric conformers of [Ag₅1₂]⁵⁺ is theoretically achieved by cleavage of coordination bonds, followed by the bowl-to-bowl inversion of corannulene and the re-association of the cage complexes, while the $P,M,P \leftrightarrows P,P,P$ and $M,P,M \leftrightarrows M,M,M$ conversions could be readily realized through twist of the cage.19a

DFT (B3LYP/CPCM-UAHF) energy minimized models of $[Ag_51_2]^{5+}$ provide a realistic illustration of the helical, D_5 -symmetric cage geometry of all the four conformers and an enantiomeric relationship between each pair of enantiomers (Table S7 and S8, SI). In the cages, five Ag⁺ cations are held between two helically-arranged ligands 1 facing each other, with the coordination angles of ca. 169° in the cases of P,M,P/M,P,M and ca. 172° in those of P,P,P/M,M,M. Due to the curvature of corranulene, the different arrangement patterns will give different torsion angles between the two corannulene units (the two corranulene units are offset by 22~23° and ca. 6° for *P*,*M*,*P*/*M*,*P*,*M* and *P*,*P*,*P*/*M*,*M*,*M* conformers, respectively). As a result, despite of possessing almost the same molecular volume, compared to P,P,P/M,M,M conformers, the *P*,*M*,*P*/*M*,*P*,*M* ones, in which the pyridyl groups tilt in the opposite direction to the helical pattern of the substitution on corranulene to balance the influence of the curvature of corranulene, are 11 kcal mol⁻¹ lower in energy. Ion-pairing with triflate anions gives a slight change in geometry of the cage due to the produced steric interaction for all conformations, which further gives rise to a decrease in the energy gap between P,M,P/M,P,M and P,P,P/M,M,M conformers (Table S7, SI). Overall, the DFT calculations predicted that the energy level of [(P,M,P/M,P,M)-Ag₅**1**₂]·[OTf]₅ lies 6~9 kcal mol⁻¹ lower in energy than that of $[(P,P,P/M,M,M)-Ag_{5}\mathbf{1}_{2}]\cdot[OTf]_{5}$, dependent on the location of counter triflate anions (Table S7, SI).

The ¹H NMR spectra of solutions of 2:5 mixtures of **1** and several metal salts, such as $[Cu(CH_3CN)_4]$ (PF₆), in common or mixed solvents exhibited complicated or no signals, even after the samples were heated. However, with Ag(OTf) as the salt, the ¹H NMR spectrum of the mixture in 93:7 (v/v) CDCl₃/CD₃CN clearly showed a set of intense, well-resolved signals that is assigned to the racemic of $[(P,M,P)/(M,P,M)-Ag_5\mathbf{1}_3]$ ·[OTf]₅ (Figure 2b and

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Figure 2. ¹H NMR spectra (600 MHz, 93:7 (v/v) CDCl₃/CD₃CN) of ligand and cages complexes. (a) ligand 1 (2 mM, 298 K); (b–c) cage [*mix*-Ag₅1₂]·[OTf]₅ (1 mM) ((b) at 298 K, (c) at 253 K); (d–e) [*mix*-Ag₅1₂]·[OTf]₅ (1 mM, 253 K) in the presence of (d) 10 equiv of Δ -TRISPHAT anions and (e) 10 equiv of Λ -TRISPHAT anions and D₂O (0.4% (v/v) accounted to CDCl₃/CD₃CN mixture). Cage [*mix*-Ag₅1₂]·[OTf]₅ was prepared by mixing 1 with 2.5 equiv of Ag(OTf). Resonances corresponding to *P*,*P*,*P* and *M*,*M*,*M* isomers were labelled in light blue dots (Figure 2b).

Figure S₃, SI) based on the results of DFT calculations.²¹ Another set of signals with much weaker intensities can also be observed. We attributed it to the P,P,P/M,M,M isomers.²¹ The assignments of the ¹H NMR signals of ligand 1 and $[(P,M,P)/(M,P,M)-Ag_{5}1_{2}] \cdot [OTf]_{5}$ were performed based on the corresponding 'H-'H NOESY, 'H-'H COSY, ¹H-¹³C HSQC, and ¹H-¹³C HMBC experiments (see Figure S7-S15, SI).²² Relative to that of 1, the pyridine protons those are located in the inner cavity of the cage, H_c, shifted far to the upfield, as a response to the strong shielding of the cage. The other two pyridyl protons, $H_{\rm b}$ and $H_{\rm d}$, downshifted due to the deshielding of the introduced metal cation. Notably, upon complexation, the methylene protons on the iso-butyl side chains, He, split into two sets, which is an important indicator of the formation of cage species in which the substituted pyridyl groups are constrained so that the protons directed inward and outward of the cage are inequivalent.²³

2D DOSY experiments indicated that the two sets of signals shown in Figure 2b belonged to species having almost the same diffusion coefficient (Figure Si8 and Si9, SI), in accordance with relationship in size between four cage species shown in Figure 1. The calculated diffusion coefficient is $(3.3~3.4) \times 10^{-10}$ m²/s, smaller than that of ligand 1 in the same solvent mixture, 4.6×10^{-10} m²/s. According to the Stokes–Einstein equation, the ratio of these two values is largely consistent with the volume ratio between the complex cages and the ligands (ca. 2.5, Table S2, SI).

Additional evidence for the formation of the cage complexes was provided by ESI-HRMS, which showed a peak for $[Ag_51_2\cdot(OTf)_4]^{i+}$ at m/z = 3127.3357 and a series of other intense peaks resulting from partial loss or addition of silver/triflate ions during the analysis (Figure S21 and Table S3, SI).

P,M,P/M,P,M≒*P,P,P/M,M,M* Conversion and Asymmetry-induction. Interconversion between *P,M,P/M,P,M* and *P,P,P/M,M,M* conformers were clearly indicated by the variable-temperature (VT) 'H NMR spectra of the cage in 93:7 (v/v) CDCl₃/CD₃CN (Figure S5, SI). With the increase of the temperature, the equilibrium shifted toward *P,P,P/M,M,M* conformers. On the contrary, decreasing the temperature gave rise to more conformers being lower in energy. At low temperature such as 253 K, only one set of signals corresponding to *P,M,P/M,P,M* species could be observed (Figure 2c).

A series of the equilibrium constants for the $P,M,P/M,P,M \leftrightarrows P,P,P/M,M,M$ interconversion at different temperatures were calculated from the molar ratio of two pairs of stereoisomers (Table S1, SI). From these constants, the standard enthalpy of reaction, $\Delta H = -10.1 \pm 0.4$ kcal mol⁻¹, and the entropy of reaction, $\Delta S = -30.3 \pm 1.3$ cal mol⁻¹ K⁻¹, were derived from the Eyring plots. At 298 K, the Gibbs free energy of reaction, ΔG , was calculated to be ~ -1.1 kcal mol⁻¹, the absolute value of which is much lower than the DFT-calculated energy gap between P,M,P/M,P,M and P,P,P/M,M,M conformations of the cage. This might be ascribed to the steric interaction between the cage and the encapsulated solvent molecules, which would inevitably present in real solution but had ignored in the DFT calculations.²⁴

We next explored the possibility of obtaining enantiomerically enriched $[Ag_51_2]^{5+}$ cages at low temperature via asymmetric induction using noncovalent chiral auxiliaries such as Δ/Λ -tris(tetra-chlorobenzenediolato)phosphate(v) (Δ/Λ -TRISPHAT) anions (Figure 3a).^{19a,25} The DFT calculations suggested that (P,M,P)- and (M,P,M)-[Ag_51_2]⁵⁺ cage still exhibited a helical, D_5 -symmetric geometry when ion-pairing with TRISPHAT anions (Figure 3b,c and Table S8). In the cage, the two ligands are offset by ~22°. Charity of the cage is induced through a steroselective interaction between two aromatic rings of the anions and the pyridyl groups on the cage (Figure 3b).

The asymmetry-inducing of chiral TRISPHAT anions were first investigated by circular dichroism (CD) spectroscopy. In the experiments, enantiopure TRISPHAT anions were added to the solution of $[mix-Ag_51_2]\cdot[OTf]_5$ (50 µM) in 93:7 (v/v) CHCl₃/CH₃CN; and the changes were recorded at 253 K. $[nBu_4N][\Delta$ -TRISPHAT] and $[nBu_3NH][\Lambda$ -TRISPHAT] were used as the TRISPHAT sources. Despite having a slight difference in structure of the countercations, these two compounds exhibit a perfect enantiomeric relationship to each other (Figure S22 and Figure S23, SI). The CD spectra associated with $[Ag_51_2]^{5+}$ cages themselves were obtained after subtraction of the corresponding TRISPHAT contributions.

In the absence of chiral anions, the cages exhibited no CD signals, as expected for a racemic mixture. With the addition of $[nBu_4N][\Delta$ -TRISPHAT], the signals appeared (Figure 4), indicative of the induction of helical bias through diastereoselective $Ag^+ \cdot [TRISPHAT]^-$ ion-pair formation. The spectrum showed a main positive peak



Figure 3. (a) Structures of Δ/Λ -TRISPHAT anions. (b-c) DFT (B₃LYP/CPCM-UAHF) energy minimized structure of $[(M,P,M)-Ag_5\mathbf{1}_2]\cdot[\Delta$ -TRISPHAT]₅ ((b) Ball (for cations) and stick diagrams; (c) space-filling representation); one C_5 and five C_2 axes presented in $[Ag_5\mathbf{1}_2]^{5+}$ architecture are shown; other TRISPHAT anions were deleted for clarity.



Figure 4. Solid lines: CD spectra (93:7 (v/v) CDCl₃/CD₃CN, 253 K) of $[mix-Ag_{5}\mathbf{1}_{2}]\cdot[OTf]_{5}$ (50 μ M) in the presence of 10 equiv of $[nBu_{4}N][\Delta$ -TRISPHAT] and that of $[nBu_{3}NH][\Lambda$ -TRISPHAT]. Contributions from TRISPHAT anions were subtracted; main fractions of the cage isomers are indicated. Dash dot lines: TD-DFT calculated CD spectra of the isolated cages $[(M,P,M)-Ag_{5}\mathbf{1}_{2}]^{5+}$ and $[(P,M,P)-Ag_{5}\mathbf{1}_{2}]^{5+}$ using the B3LYP//LANL2DZ/6-31G(d) and the CPCM model for 93:7 (v/v) CDCl₃/CD₃CN (further details are described in Section 7, SI). The calculated spectra are vertically scaled.

at 290 nm, accompanying two shoulder-peaks at 265 and 326 nm, respectively, and a main negative one at 370 nm. In the presence of 10 equiv of Δ -TRISPHAT, the apparent CD anisotropy factor, g, of the cage was calculated to be 1.6×10⁻³ and 2.7×10⁻³ at 290 nm and 370 nm, respectively. Time-dependent (TD) DFT calculations suggest that

(M,P,M)- $[Ag_5\mathbf{1}_2]^{5^+}$ should exist predominantly over the P,M,P ones under such condition (Figure 4). As expected, with $[nBu_3NH][\Lambda$ -TRISPHAT], the induced CD spectrum showed a mirror image as well as the same g values as those in the case of Δ -TRISPHAT (Figure 4 and Table S4, SI). Besides, cage (P,M,P)- $[Ag_5\mathbf{1}_2]^{5^+}$ prevails in this case, according to the results of TD-DFT calculations (Figure 4). It is noteworthy that the TD-DFT-calculated ECD spectra of $[(P,P,P)-Ag_5\mathbf{1}_2]^{5^+}$ and $[(M,M,M)-Ag_5\mathbf{1}_2]^{5^+}$ do not agree well with that of experimental ones (Figure S49), confirming the absence of P,P,P/M,M,M conformers in our asymmetric induction experiments.

To get deeper insights into the asymmetry-induction of the chiral anions, we next carried out the 'H NMR titration experiments. Upon addition of $[nBu_4N][\Delta$ -TRISPHAT] to the racemic mixture (1 mM) in 93:7 (v/v) CDCl₂/CD₂CN at 253 K, a new set of signals mainly corresponding to $[(M, P, M) - Ag_5 \mathbf{1}_2] \cdot [\Delta - TRISPHAT]_5$ appeared (Figure 2d and Figure S₃₂, SI), in which the signal of protons those in proximity to the counter anions, H_d, shifted upfield dramatically owing to the greater shielding effect imparted by the chiral anions. Clearly, the ion-association of $Ag^{+} \cdot [\Delta$ -TRISPHAT]⁻ ion-pair is much stronger than that of $Ag^+ \cdot (OTf)^-$, giving that the new cage complexes equilibrate slowly on the NMR time scale with all previous species, including [mix-Ag₁]·[OTf]₅ and the solvated [mix- Ag_{s1} , $[OTf]_{s}$. The $[(M,P,M)/(P,M,P)-Ag_{s1}] \cdot [OTf]_{s} \Leftrightarrow$ $[(M, P, M) - Ag_{5}\mathbf{1}_{2}] \cdot [\Delta - TRISPHAT]_{5}$ reaction involves fivesteps of ion-exchange. Assuming that the ion-exchange process for each step is completely independent from the others, the equilibrium constant for the ion-exchange $[(1/5) \cdot mix - Ag_5 \mathbf{1}_2]^+ \cdot [OTf]^ [\Delta$ -TRISPHAT]⁻ + ⇆ $[(1/5)\cdot(M,P,M)-Ag_{5}\mathbf{1}_{2}]^{+}\cdot[\Delta-TRISPHAT]^{-} + [OTf]^{-}$ was calculated to be 2.3 \pm 0.5 (Table S6, SI). The stronger ionpairing with Δ -TRISPHAT anions may probably be attributed to the formation of π - π and/or halogen- π ²⁶ interactions between TRISPHAT anion and the two pyridyl groups bridged by Ag⁺ cation. On the other hand, the fact that only one set of signals could be observed indicates that the cage complexes interconvert rapidly between the P,M,P and M,P,M conformers on the NMR timescale.^{19a} Ascribed to the enantiomeric nature, addition of $[nBu_3NH][\Lambda$ -TRISPHAT] gave rise to very similar results as those in the case of Δ -TRISPHAT (Figure 2e and Figure S33, SI), except that less amount (5 equiv) of TRISPHAT was needed to saturate the anion exchange compared to that in the case of $[nBu_4N][\Delta$ -TRISPHAT] (8 equiv). The equilibrium constant for $[(1/5)\cdot mix-Ag_5\mathbf{1}_2]^+ \cdot [OTf]^- + [\Lambda$ - $TRISPHAT]^{-} \simeq [(1/5) \cdot (P, M, P) - Ag_{5}\mathbf{1}_{2}]^{+} \cdot [\Lambda - TRISPHAT]^{-} +$ $[OTf]^-$ was calculated to be 10.5 ± 3.1 (Table S6, SI). This indicates that the use of TRISPHAT anion as a *n*Bu₃N⁺H salt leads to the formation of a more tightly associated $Ag^+ \cdot [TRISPHAT]^-$ ion-pair compared to that as a nBu_4N^+ one, probably due to that nBu_2N^+H is more strongly solvated under the studied condition.

An interesting question arising from above ¹H NMR titration experiments is how the *P*,*M*,*P* \leftrightarrows *M*,*P*,*M* conversion occurs while [Ag₅**1**₂]⁵⁺ is ion-pairing with the chiral anions. It is worth noting that, in solution, the Δ/Λ -TRISPHATcage complexes may exist as three kinds

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Figure 5. Schematic illustration of the interconversion between (M,P,M)- $[Ag_51_2]_{5+}$ and (P,M,P)- $[Ag_51_2]^{5+}$ cages, which take place when the cages are loosely associated with the chiral TRISPHAT anions (as an example, a solvent-shared model is shown). Solvent molecule is labelled with "S".

of ion pairs,²⁷ including tight, solvent-shared and solventseparated ones.²⁸ Therefore, interconversion between the diasteromeric P,M,P- and M,P,M-type helical cage may possibly occurs at any above states. However, DFT calculations indicated that the energy level of the ground state conformation of contacted $[(P, M, P) - Ag_5 \mathbf{1}_2] \cdot [\Delta -$ TRISPHAT]₅ is 13 kcal mol⁻¹ higher in energy than that of [(M, P, M)-Ag₅1₂]·[Δ -TRISPHAT]₅ (Table S7 and Table S8, SI). This suggests that a two way $P,M,P \leftrightarrows M,P,M$ conversion in fact more likely take place when the cages are loosely associated (including solvent-shared and solventseparated ion-pairing) with the chiral anion (Figure 5). This is understandable because looser association would give a much lower enantiomerization barrier of the complexes.

Increasing temperature leads to the formation of more loosely associated ion pairs thus giving rise to a decrease in the asymmetry-induction ability of the chiral anions. This was evidenced by the VT CD measurements, which showed that the CD signals of TRISPHAT-paired cages gradually decreased upon increasing temperature and completely disappeared at 333 K (Figure S28-S31, SI). Corresponding VT 'H NMR investigation showed that increasing temperature from 253 K produced continuous downfield shift of proton H_d (Figure S35-S36, SI), indicating that tight $Ag^{\dagger} \cdot [\Delta/\Lambda - TRISPHAT]^{-}$ ion-pairing kept turning into loose ones in this process which agrees well with the results of VT CD measurements. Overall, the P,M,P/M,P,M conformations in such cases were found to be more stable than those in the case of OTf-paired cages: at least at 303 K, there was still only one set of signals mainly corresponding to $[(M,P,M)-Ag_{51_2}]\cdot [\Delta$ -TRISPHAT]₅ that could be observed (compared to that should be lower than 263 K in the case of $[mix-Ag_51_2] \cdot [OTf]_5$; Figure S5); $[(P,M,P)-Ag_{1}]\cdot [\Lambda$ -TRISPHAT]₅ can even stand higher temperature. The higher energy barriers of P,M,P/M,P,M $rac{} P, P, P/M, M, M$ interconversions are attributed to the stronger Ag⁺· $[\Delta/\Lambda$ -TRISPHAT]⁻ ion-pairing, which may enlarge the energy gap between P,M,P/M,P,M conformers

and P,P,P/M,M,M ones or increase the energy level of the transition state (wherein all the N–Ag–N linkages are parallel to the helix axis)^{19a} of the flips.

We finally explored the asymmetry-induction with non- enantiopure anions, by measuring 'H NMR and CD spectra of $[Ag_{5^{1_2}}]^{5^+}$ with the mixtures of $[nBu_4N][\Delta$ -TRISPHAT] and $[nBu_3NH][\Lambda$ -TRISPHAT] at a constant 10 times total concentrations to that of the cages. The 'H NMR spectrum did not show obvious changes upon changing the ratios of two chiral anions (Figure S45, SI). The CD spectrum changed as expected (Figure 6a), but the intensity was not linearly proportional to the enantiomeric excess (e.e.) of the mixture (Figure 6b). This indicates that, to some extent, the major enantiomer of TRISPHAT anions controls the bias of helical sense of $[Ag_51_2]^{5^+}$ cages. Such "majority rules" has been widely observed in many supramolecular interaction systems.²⁹



Figure 6. (a) CD spectra (93:7 (v/v) CHCl₃/CH₃CN, 253 K) of $[Ag_5I_2]^{5+}$ cages (50 μ M) obtained from different ratios of Δ - and Λ -TRISPHAT anions. (b) Corresponding plots of CD spectral intensities against e.e.'s of TRISPHAT anions.

CONCLUSIONS

A new supramolecular helical cage that based on the coordination of metal cations to corannulene-based ligands has been designed and synthesized. The cage exists as an ensemble of four stereoisomers, i.e., two pairs of enantiomers, at ambient and elevated temperatures, which is much different from that of the traditional Ag_xL₂-type ones. Owing to the dynamic, switchable molecular chirality of the corannulene moiety, decreasing the temperature gave finally the presence of only one pair of enantiomers. Further, with the help of asymmetryinduction using chiral TRISPHAT anions, helical sense bias for the cage could be efficiently achieved. The finding verifies that the corannulene moiety can indeed provide molecular cages distinctive conformational and dynamic characteristics compared to traditional ones. The constructed cage extends the applications of the bowl-shaped polycyclic aromatic hydrocarbons and would potentially expand the geometric diversity of artificial molecular cages. We envisage that the cage might find applications in chiral molecular recognition or preparation of functional materials with chiroptical properties.

EXPERIMENTAL SECTION

General Information. All starting chemicals were obtained from commercial sources and used without further purification, unless indicated otherwise. Anhydrous toluene was dried from sodium/benzophenone and then distilled under inert atmosphere, while anhydrous dichloromethane (DCM) was distilled over calcium hydride (CaH₂), respectively. Anhydrous dimethyl sulfoxide (DMSO) was obtained from commercial sources. Corannulene was provided by Prof. Jay S. Siegel at School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, China. [Tetrabutylammonium][Δ -tris(tetrachloro-1,2-benzenediolato)phosphate(V)] (Δ -TRISPHAT tetra-butylammonium salt, [nBu_4N][Δ -TRISPHAT]) was obtained from commercial sources; the enantiomer, [nBu_3NH][Λ -TRISPHAT], was prepared according to the procedure reported in the literature²⁵.

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Analytical TLC was carried out using tapered silica plates with a preadsorbent zone. Crude compounds were purified by flash column chromatography, using flash grade silica gel and o - 20 psig pressure, performed at ambient pressure. Perdeuterated solvents for NMR spectroscopy were obtained from Cambridge Isotope Laboratories and used as received. NMR spectra were obtained with a Bruker spectrometer (¹H, 400, 500, and 600 MHz) or a JEOL Delta spectrometer (¹H, 400 and 600 MHz) using chloroform-d (CDCl₃), acetonitrile d_3 or the mixture of them as solvent. The chemical shift references were as follows: ('H) chloroform, 7.26 ppm (chloroform-d), (¹³C) chloroform-d, 77.16 ppm (chloroform-d); (¹H) acetonitrile- d_3 , 1.94 ppm (acetonitrile- d_3), (¹³C) acetonitrile- d_3 , 118.26 ppm (acetonitrile-*d*₃); (¹H) 1,1,2,2-tetrachloroethane-*d*₂, 6.00 ppm (1,1,2,2-tetrachloroethane- d_2 , $({}^{13}C)$ 1,1,2,2tetrachloroethane- d_2 , 73.8 ppm (1,1,2,2-tetrachloroethane- d_2). (¹H) tetramethylsilane (TMS), o.oo ppm (the mixture of chloroform-d and acetonitrile-d3). Typical 1D FID was subjected to exponential multiplication with a line broadening exponent (LB) of 0.3 Hz (for ¹H) and 1.0 Hz (for ¹³C). 2D NOESY was recorded with the mixing time of 300 ms. UV-vis spectra were obtained on Shimadzu (UV-2401PC) spectrophotometer, using 10-mm or 1-mm path-length quartz cells. Circular dichroism (CD) spectra were obtained using ChirascanTM spectropolarimeter (Applied Photophysics Ltd., United Kingdom), equipped with a Peltier temperature controller. In cases that temperatures lower than 253 K (-20 °C) were needed, an add-on recirculating chiller was used. 1-mm pathlength quartz cells were used in all the CD measurements. For Both UV-vis and CD, the mixture (93:7 (v/v)) of spectrophotometric grade chloroform ($\geq 99.8\%$) and acetonitrile $(\geq 99.5\%)$ was used as the solvent. Optical rotations were measured with Autopol III (Rudolph Research) at ambient temperature, using ethanol as the solvent. The measurements were repeated for five times; specific rotation was calculated based on the mean value of the measured rotation in degrees. IR spectra were recorded on FTIR Spectrometer (IR Affinity-1) with thin KBr disk. 128 scans were acquired, with a resolution of 2 cm⁻¹. Exact mass spectra (EI, ESI, MALDI) were acquired on GCT, FT-ICR spectrometer.

3-Bromo-5-*iso***-butoxypyridine** (2): To a solution of 5bromopyridin-3-ol (3.0 g, 17.24 mmol, 1.0 equiv) in DMF (15 mL), 1-iodo-2-methylpropane (2.2 mL, 18.96 mmol, 1.1 equiv) and K₂CO₃ (3.57 g, 25.86 mmol, 1.5 equiv) was added. The suspension mixture was stirred at 60 °C for overnight and then poured into pure water, then extracted with ethyl acetate. The organic layer was washed with brine for more than 5 times to remove the contained DMF, dried over sodium sulfate and concentrated in vacuo. The residue was purified on silica gel flash column chromatography (ethyl acetate/hexane, 1:15) to give the product **2** as a pale yellow oil (2.58 g, yield: 65%). R_f = 0.6 (ethyl acetate/hexane, 1:15). IR (KBr, cm⁻¹): 2960, 2925, 1575, 1425, 1260, 1100, 1020, 800. ¹H-NMR (400MHz, CDCl₃): δ = 8.26 (s, 1H), 8.23 (s, 1H), 7.347.35 (t, J = 2.4 Hz, 1H), 3.75 (d, J = 6.8 Hz, 2H), 2.10 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H) ppm; ¹³C NMR (100MHz, CDCl₃): $\delta =$ 155.8, 142.7, 136.6, 123.8, 120.4, 75.0, 28.2, 19.1 ppm. TOF-HRMS-ESI (1% HCOOH in MeCN, ion type, % RA for m/z): Calcd. for C₉H₁₃BrNO at [M+H]⁺: 230.0181 (100.0%), 231.0214 (9.7%), 232.0160 (97.3%, 2.6 ppm), 233.0194 (9.5%); Found: 230.0176 (100.0%, 2.2 ppm), 231.0211 (8.7%, 1.3 ppm), 232.0154 (97.9%, 2.6 ppm), 233.0185 (8.5%, 3.9 ppm).

3-iso-Butoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (3): We followed the previously published procedure³⁰ for preparation of the compound. To starting 8.7 mmol, material 2 (2.0 g, 1.0 equiv), bis(pinacolato)diboron (2.43 g, 9.56 mmol, 1.1 equiv), Pd(dppf),Cl, (191 mg, 0.26 mmol, 0.03 equiv) and KOAc (2.56 g, 26.1 mmol, 3 equiv) in 50 mL double-necked flask prefilled with argon, anhydrous DMSO (Acros, 15 mL) was added. The mixture was stirred at 80 °C for 8 h, poured into brine and then extract with dichloromethane. The combined organic layer was washed with brine for three times, dried over sodium sulfate and concentrated on rotary evaporator to give a black viscous crude oil. The oil was washed with *n*-hexane and filtered. The filtrate was concentrated and dried in vacuo to give a yellow oil (1.94 g, yield: 80%) which was directly used for the next step reaction without further purification. IR (KBr, cm⁻¹): 2980, 2930, 2875, 1600, 1450, 1370, 1160, 1040, 850. ¹H NMR (400MHz, CDCl₂): $\delta = 8.52$ (d, I = 1.2 Hz, 1H), 8.35 (d, J = 3.2 Hz, 1H), 7.52 (dd, J = 1.2 Hz, 3.2 Hz, 1H), 3.77 (d, J = 6.4 Hz, 2H), 2.10 (m, 1H), 1.35 (s, 12H), 1.02 (d, J = 7.6 Hz, 6H) ppm; ¹³C NMR (100MHz, CDCl₃): δ = 155.2, 147.4, 140.9, 126.23, 84.3, 82.7, 28.4, 24.9, 19.2 ppm. TOF-HRMS-ESI (1% HCOOH in MeCN, ion type, % RA for m/z): Calcd. for $C_{15}H_{24}BNNaO_{2}$ at $[M+Na]^{+}$: 300.1747 (100.0%), 299.1783 (24.87%), 300.1780 (16.23%); Found: 300.1744 (100.0%, 1.0 ppm), 299.1788 (24.0%, 1.7 ppm), 300.1772 (16.3%, 2.7 ppm).

1,3,5,7,9-Pentachlorocorannulene (4). The procedure was slightly modified from the one previously reported in the literature.³¹ To a solution of iodine monochloride (ICl, Aldrich, 21 mL, 1.0 M, 21 mmol, 13.0 equiv) in dichloromethane at -78 °C, corannulene powder (400 mg, 1.60 mmol, 1.0 equiv) was added under a positive pressure of argon. The resulting purple suspension was warmed slowly to room temperature over 10 h, then stirred at ambient temperature for an additional 72 h. The solution was poured into 50 mL of chloroform and washed with 5% aqueous sodium thiosulfate (20 mL \times 2) and pure water (20 mL \times 2). The resulting yellow suspension was evaporated to dryness and triturated 2 times with hexanes (20 mL) and 3 times with dichloromethane (10 mL). The resulting yellowish solid was recrystallized from 1,1,2,2-tetrachloroethane to yield a pale yellow solid (335 mg, yield: 50%). M.p. (under air): 432–434 °C. IR (KBr, cm⁻¹): 1610, 1420, 1300, 1175, 910, 875. ¹H NMR (400 MHz, 25°C, $C_2D_2Cl_4$): δ = 7.99 (s, 5H) ppm; ¹³C NMR (150 MHz, $C_2D_2Cl_4$, 100°C): not obtained due to its poor solubility under the measured condition. HRMS-MALDI-TOF: Calcd. for $C_{20}H_6Cl_5$ at $[M+H]^+$: 422.8883 (100%), 424.8853 (63.9%), 420.8912 (62.58%), 423.8916 (21.63%), 425.8887 (13.83%), 421.8946 (13.54%); Found: 422.8856 (100%, 6.4 ppm), 424.8842 (63.58%, 2.6 ppm), 420.8872 (62.38%, 9.5 ppm), 423.8902 (21.57%, 3.3 ppm), 425.8895 (13.91%, 1.9 ppm), 421.8926 (13.04%, 4.7 ppm).

1,3,5,7,9-Penta-(5-iso-butoxy-3-pyridinyl)corannulene (1): Starting material 1,3,5,7,9-penta-chlorocorannulene (4) (100 mg, 0.24 mmol, 1.0 equiv) was taken to a Schlenk vessel and evacuated under high vacuum at ambient temperature

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for 1 h. The Schlenk vessel was charged with argon. Then to this Schlenk vessel in an argon glove bag, compound 3 (825) mg, 2.98 mmol, 12.5 equiv) and $Pd(PPh_3)_4$ (82 mg, 0.07 mmol, 0.3 equiv) was added. The mixture was evacuated under high vacuun for 2 h and charged with argon again. To the vessel, degassed solvents (degassed by continuous bubbling of argon gas), benzene (8 mL), EtOH (4 mL), and aqueous K₃PO₄ solution (2 M, 8 mL) were added. The mixture was degassed again by freeze-pump-thaw method. (In this process, the reaction mixture was rapidly frozen under vigorous stirring to ensure that the solidified mixture was still phase separated, 10 to minimize the probability of glassware breakage.) The mix-11 ture was stirred for 15 minutes at room temperature, then at 12 100 °C for 6 days. The mixture was cooled down to room 13 temperature. Most of the solvent was removed; water (10 mL) was added and the crude product was extracted with chloro-14 form $(2 \times 10 \text{ mL})$. The organic layers were concentrated un-15 der reduce pressure and then redisperse into toluene (2 mL). 16 The insoluble solid was collected and washed with toluene (2 17 \times 2 mL), methanol (2 \times 2mL) and acetonitrile (2 \times 2 mL), 18 affording pure product 1 as a pale yellow solid (118.5 mg, yield: 19 50%). M.p. = 295–297 °C. IR (KBr, cm^{-1}): 3050, 2960, 2925, 20 2870, 1600, 1560, 1425, 1310, 1210, 1160, 1050, 860. ¹H NMR 21 $(400 \text{ MHz}, \text{ CDCl}_3)$: $\delta = 8.49 \text{ (d, } J = 1.6 \text{ Hz}, 5\text{H})$, 8.40 (d, J = 2.8 Hz, 5H)22 Hz, 5H), 7.81 (s, 5H), 7.47 (t, J = 2.4 Hz, 5H), 3.84 (d, J = 6.4 23 Hz, 10H), 2.10 (m, 5H), 1.03 (d, J = 6.8 Hz, 30H) ppm; ¹³C NMR (100MHz, CDCl₂): δ = 155.5, 142.6, 139.2, 137.2, 135.9, 24 135.5, 129.4, 126.5, 122.5, 75.0, 28.4, 19.3 ppm. HRMS-FTMS (1% 25 HCOOH in MeCN, ion type, % RA for m/z): Calcd. for 26 $C_{65}H_{66}N_5O_5$ at $[M+H]^+$: 996.5064 (100%), 997.5097 (70.32%), 27 998.5131 (24.34%); Found: 996.5073 (100%, 0.9 ppm), 28 997.5086 (83.56%, 1.1 ppm), 998.5100 (20.38%, 3.1 ppm). 29

ASSOCIATED CONTENT

SUPPORTING INFORMATION

The Supporting Information is available free of charge on the ACS Publications website.

> Experimental and computational details and characterization data, including spectra for NMR and CD investigation on the asymmetry induction (PDF)

AUTHOR INFORMATION

CORRESPONDING AUTHOR

* jiangh@bnu.edu.cn

- *<u>xuebochen@bnu.edu.cn</u>
 - ywangi@bnu.edu.cn

Author Contributions

[#]F.H. and L.M. contributed equally to this work.

NOTES

The authors declare no competing financial interests.

ACKNOWLEDGMENT

The National Natural Science Foundation of China (21332008, 21572023 and 21672026) and the 973 Program (2015CB856502) are acknowledged for financial support. We thank Prof. Jay S. Siegel for providing the starting material, corannulene.

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