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Article

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Geminiarene: Molecular Scale Dual Selectivity for Chlorobenzene and Chlorocyclohexane Fractionation

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Supporting Information Placeholder

ABSTRACT: In this work, a new version of macrocyclic arenes, namely geminiarene, has been designed and synthesized for guest complexation and chlorobenzene/chlorocyclohexane mixture separation with excellent dual selectivity. Due to its unique dual/gemini conformational feature, not only chlorocyclohexane can be separated from chlorobenzene with exceeding 97% purity, but also chlorobenzene can be separated from chlorocyclohexane with purity over 88%, and the dual selective fractionation process could be achieved in only one cycle of operation. Significantly, we demonstrate that the dual selectivity capability is essentially a competition of the stability between the guest-free and guest-loaded crystalline phases of geminiarene. We strongly believe that this work and the idea of multiple selective separation systems will open up new perspectives on macrocycle-based solid-state host-guest chemistry and molecular scale separation materials.

INTRODUCTION

The creation and development of various molecular containers is the core of research subject in host–guest and supramolecular chemistry during the past 50 years,[1,2] among which, prevalent macrocyclic compounds, that is, crown ethers, cyclodextrins, calixarenes, cucurbiturils, and pillar[n]arenes (pillarenes for short), are the most representative examples.[3] Function-directed macrocyclic derivatives design and synthesis endows them great contribution to different research fields, including but not limited to host–guest binding, molecular machinery, extraction and separation, and biomimetics.[4,5] Interestingly, the development of synthetic macrocycles has gradually transformed into an application-oriented molecular design and synthesis instead of the traditional structure-directed functional establishment, and numerous examples support this view.[6,7] For instance, leaning pillar[6]arene, a new version of macrocyclic arenes, was first introduced by us in 2018, aiming at increasing the cavity flexibility and enhancing the binding properties of traditional pillarenes.[7a] In 2019, Davis and coworkers reported a biomimetic macrocycle receptor, which was designed and synthesized for highly selective glucose binding.[7f] Hence, instead of being stuck at the stage of serendipitous discovery and simple fondness for macrocycle synthesis, ingenious design rooted within some special vocations have become the theme for modern synthetic macrocyclic chemistry.

It is well known that nearly all function development based on macrocycles were carried out in solvent system, thus, macrocycle-based solid-state host–guest chemistry investigations are always one of the frontier science and hotspots, cross over many supramolecular research fields and beyond.[8] In the last few years, pillarene-based molecular crystal materials have been given broad attention in virtue of their high selectivity, ease of preparation, nice chemical stability, solubility, and indeed recyclability.[9,10] Thus, the reality exists and complicated separation problems have been successfully and ideally resolved in laboratory. In 2014, we reported the first pillarene-based supramolecular organic porous crystal material, which showed high selectivity and reversible adsorption toward CO_2 in ambient condition.[9] Afterward, Huang, Ogoshi, Cooper et al. reported pillarene-based adaptive crystal materials, where dense packing and guest-free pillarene crystalloids were easily penetrated by preferable guest molecules through solid-liquid or solid-vapor contact, achieving selective guest separation and adsorption.[10]

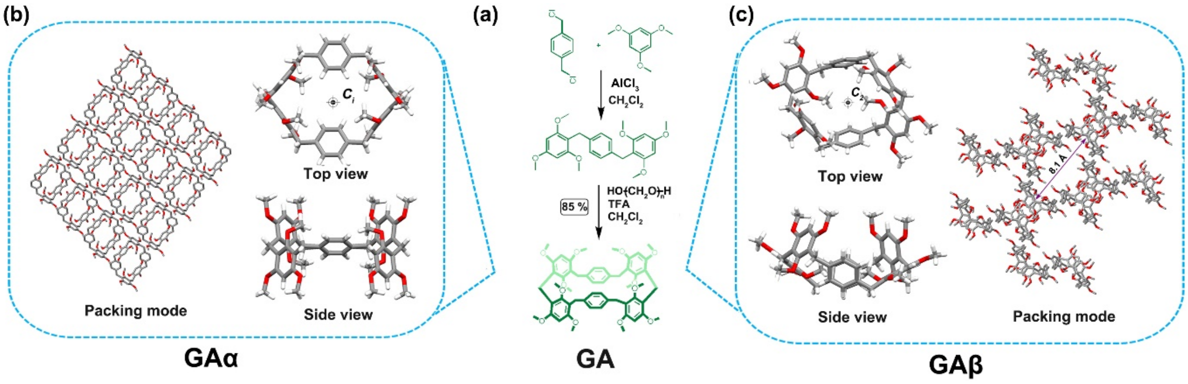


Figure 1. (a) Synthetic route to geminiarene (**GA**). Single-crystal structures of (b) **GAα** and (c) **GAβ** obtained from different conditions.

As a typical type of macrocycle-based material, pillarene crystals have great potentials in adsorption and separation, however, there are still many objective challenges or limitations remained to be solved or enhanced: (i) perethylated pillar[6]arene (EtP6A) is the most frequently used pillarene homologue to construct crystal materials owing to its nice cavity adaptability and flexibility. However, EtP6A usually cannot be prepared on a large scale and always accompanies with complicated separation and purification procedures,[3f,11] thus, it may be far away from the practical use; (ii) Due to the cavity-size limitation, 1:1 or 1:2 solid-state host–guest complexes are always observed in pillarene crystals, and strongly limit its separation capacity and efficiency; (iii) mono-activated crystalline phase makes the pillarene always presented single selectivity during the separation process, in other words, only one component can be separated from a mixed system by one type of pillarene molecular crystals.[10]

The separation of aliphatic cyclic compounds from corresponding aromatic compounds has been listed as one of the difficult separation subjects due to their similar physical properties.[12] Chlorobenzene (**CB**), a chlorinated aromatic organic compound, is frequently used as an organic solvent, starting reagent, and organic synthesis intermediate in chemical industry.[13] However, **CB** can cause serious harm to the environment and human health as a result of its strong bioaccumulation, acute toxicity, and chemical stablility.[14] Besides, to some extent, **CB** also contributes to global warming and ozone depletion. So, it's necessary to convert it to alternative compounds that are environmentally acceptable or reusable before discharge.[15] By hydrogenation or electrochemical degradation of **CB**, chlorocyclohexane (**CCH**), a less harmful chlorinated aliphatic cyclic compound and useful pharmaceutical intermediate, could be obtained.[16] But, due to their similar boiling points (**CB** 132 °C， **CCH** 142 °C), it is unrealistic to use the traditional separation methods, such as distillation, to separate **CCH** with high purity from the unreacted **CB**.

Here we report a new class of supramolecular macrocyclic arene, referred to as geminiarene (**GA**), named by us according to its two superficially different but actually interconvertible solid-state configurations (referred to as **GAα** and **GAβ**). Besides, **GA** combines the virtues of low cost, ease of synthesis, high preparation yield, well-defined structure, and superior crystal-state host–guest properties. Most importantly, **GA** possesses the capability in dual selective mixture separation as a result of its two conformational structures naturally with different guest binding preferences. Taking the **CB**/**CCH** mixture separation as an example, **GA** could separate **CCH** from **CB** with more than 97% purity, while, also can separate **CB** from **CCH** with a purity over 87%, and both the selective separation could be realized in one single cycle, thus, molecular scale fractionation process for **CB**/**CCH** mixture could be facilely achieved.

RESULTS AND DISCUSSION

Synthesis, structural analysis and crystal-state host–guest investigation of GA. A facile two-step synthetic approach for **GA** was adopted: 1,3,5-trimethoxybenzene was reacted with 1,4-bis(chloromethyl)benzene catalyzed by $AlCl_3$ in a Friedel-Crafts alkylation reaction, giving the coupling precursor 1,4-bis(2,4,6-trimethoxybenzyl)benzene in a yield of 45%; then, the Bronsted acid-catalyzed fragment coupling method by reaction of 1,4-bis(2,4,6-trimethoxybenzyl)benzene with excess paraformaldehyde in the presence of trifluoroacetic acid led to the formation of **GA** in an excellent yield of 85 % (Figure 1a). The best reaction time would be 30-40 min at ambient temperature, and prolonged reaction time will increase the yields of oligomers and polymers thus decrease the yield of **GA**.

GA was fully characterized by NMR spectroscopy, MALDI-TOF-MS analyses as well as X-ray single-crystal diffraction (Figures S1-S6, Tables S1-S3), among which, two guest-free single crystals, that is, **GAα** and **GAβ**, with completely different molecular conformations including symmetrical characteristics, packing modes and space groups have been first obtained (Figures 1b-c). **GAα** possesses a rigid hexagon structure (C_i symmetry) (Figure 1b, right), in which the four trimethoxybenzene units are almost perpendicular to the plane of methylene bridges (Figure S7a) and the unsubstituted phenylene rings (Figure S7b). Considering the plane established by the methylene bridges, two adjacent trimethoxybenzene units point at the opposite direction respectively, giving an torsion angle of ca. 163° (Figure S8a), meanwhile, the two phenylene units are parallel to each other and tilted to the same direction (Figure S8b), and all these components leading to the regular ladder-shaped structure of **GAα** with a dense packing mode (Figure 1b, left). Completely different from **GAα**, the four trimethoxybenzene units of **GAβ** all point above the plane of methylene bridges, rendering a distorted bowl-shaped structure (C_2 symmetry) (Figure 1c, left). Besides, the unsubstituted phenylene units are no longer parallel with each other as a result of the desymmetrical molecular configuration of **GAβ**. Interestingly, each molecule in **GAβ** further interacts with twelve near neighbors through multiple C-H···O and aromatic π-π interactions (Figure S9), presenting a layer-by-layer packing modes with infinite 1D channels (Figure 1c, right). Additionally, the cavity of **GAα** is about 8.5 Å in width and 4.7 Å in height, and accordingly the diameter of the incircle of **Gaβ** is ca. 4.3 Å, which are all defined by measuring the distances between the corresponding carbon atoms after subtracting the Van der Waals radii(Figure S10).

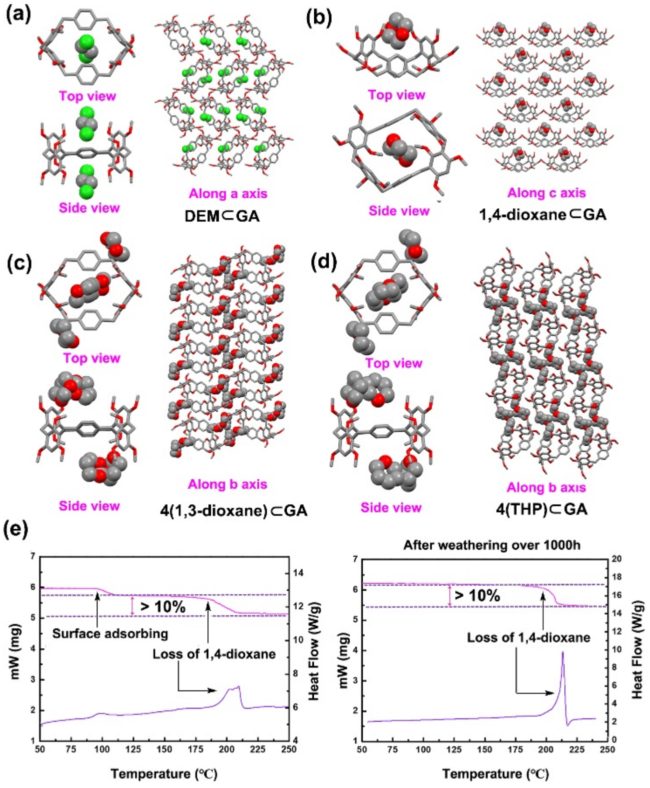
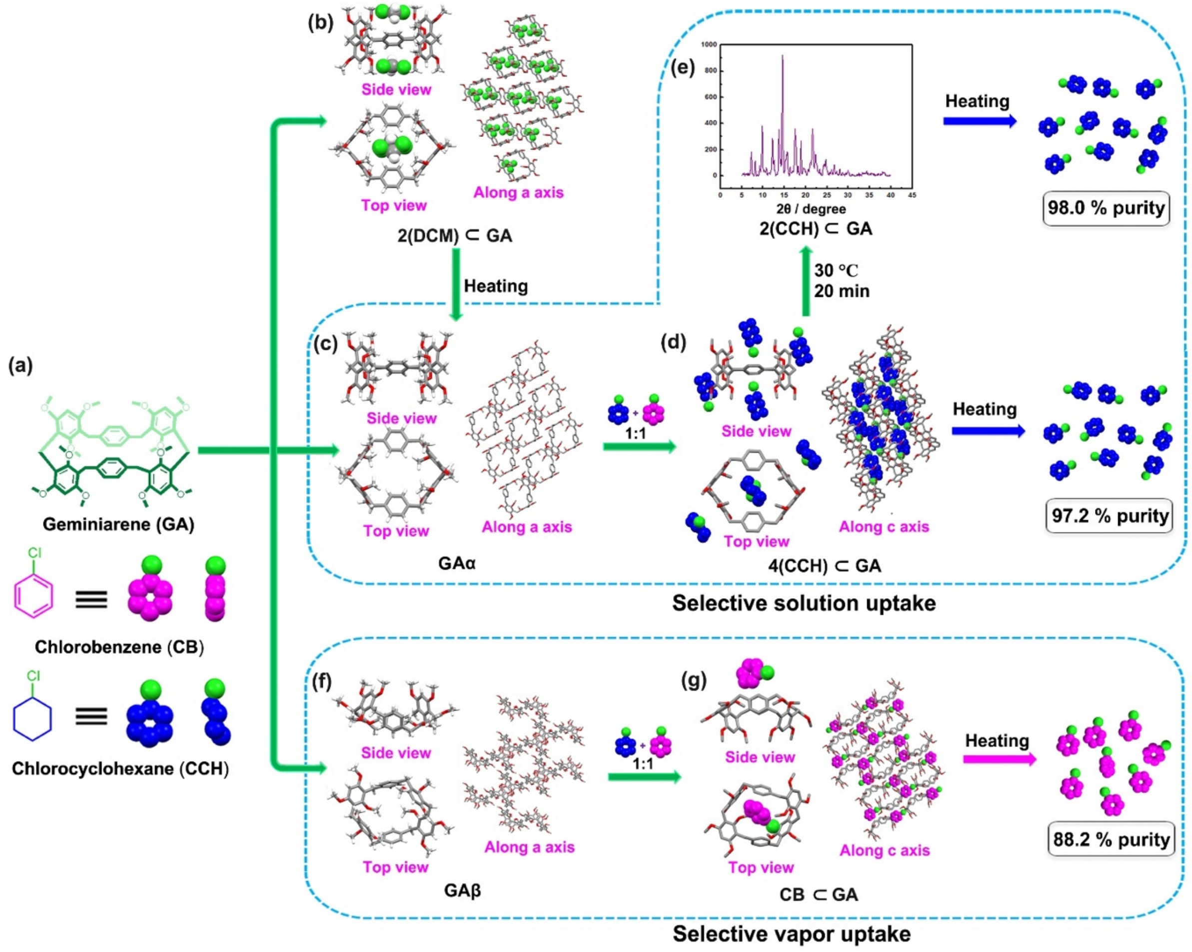


Figure 2. X-ray single-crystal structures of (a) DEM⊂**GA**, (b) 1,4-dioxane⊂**GA**, (c) 4(1,3-dioxane)⊂**GA**, (d) 4(THP)⊂**GA**. (e) TGA and DSC studies of 1,4-dioxane⊂**GA**: (left) tested without natural weathering, (right) tested after natural weathering over 1000 hrs.



Scheme 1. Interconversion of the various **GA**-based single crystal structures in solution and the solid state. (a) Chemical structure of geminiarene (**GA**), chlorobenzene (**CB**), and chlorocyclohexane (**CCH**). Single crystal structures of (b) 2(DCM)⊂**GA**, (c) **GAα**, (d) 4(**CCH**)⊂**GA**, (f) **GAβ**, (g) **CB**⊂**GA**. (e) After heating 4(**CCH**)⊂**GA** at 30 °C for 20 min, a stable intermediate state crystalline phase, referred to as 2(**CCH**) ⊂**GA**, is obtained, as confirmed by its PXRD pattern.

Besides **GAα** and **GAβ**, a series of crystal-state **GA**-based host–guest complexes were also facilely obtained, and to our surprise, not only the lipophilic species, such as the dichloromethane (DEM) and 1,2-dichloroethane (DCM) (Figures 2a, S11, referred to as 2(DCM)⊂**GA** and 2(DEM)⊂**GA**, but also many hydrophilic organic compounds, including but not limited to 1,4-dioxane, 1,3-dioxane and tetrahydropyrane (THP) (Figures 2b-d, referred to as 1,4-dioxane⊂**GA**, 4(1,3-dioxane)⊂**GA** and 4(THP)⊂**GA**), can be stably hosted, which proves that this newly designed macrocyclic arene indeed possesses a wide range of guest binding capability. More than that, there are several bright points should be paid special attention. First, compared to nearly all the famous phenol-aldehyde related macrocyclic compounds, such as calixarene and pillarene, stoichiometries of 1:1 and 1:2 are the most common host–guest binding forms in the crystal state. However, unusual 1:4 complexes are quite common in **GA** host–guest complex crystals. Second, despite of various packing modes in these binding crystals, **GA** molecules can only exist in two conformations, that is, either **GAα** or **GAβ**, further demonstrating the dual/genimi nature of **GA**. Moreover, upon analyzing the crystals of 1,4-dioxane⊂**GA**, 4(1,3-dioxane)⊂**GA** and 4(THP)⊂**GA**, we can easily figure out that slight differences from the guest species, such as molecular polarity or the position/number of the hydrogen-bond acceptors (oxygen atom), can induce the inversion of the two conformations, that is, the crystal polymorphs of **GA** are interconvertible and guest stimuli-responsive.

Additionally, 1,4-dioxane, a frequently used organic solvent and also a common byproduct in chemical and cosmetic industry, has been listed among the possible carcinogenic chemicals (Group 2B) by the International Agency for Research on Cancer,[17] and it cannot be absorbed or degraded by soil due to its high hydrophilicity. So, 1,4-dioxane must be rationally used and carefully stored. According to the thermogravimetric (TG) and differential scanning calorimetry (DSC) measurements of 1,4-dioxane⊂**GA** (Figures 2e, left), 1,4-dioxane molecules are highly stably hosted, and its release from 1,4-dioxane⊂**GA** (weight loss) started at ca. 180 °C, which is approximately 80 °C higher than its boiling point (101 °C). Most importantly, the molecular crystals of 1,4-dioxane⊂**GA** possess excellent weathering resistance capability, as depicted in Figures 2e and S12-14, no obvious loss of the trapped 1,4-dioxane molecules and crystalline phase transformation of **GA** were found even after weathering the binding crystalloids over 1000 hours at room temperature in an open cell vial with air flow, which suggests that GA has great potentials in the adsorption, purification, and especially highly stable storage of 1,4-dioxane.

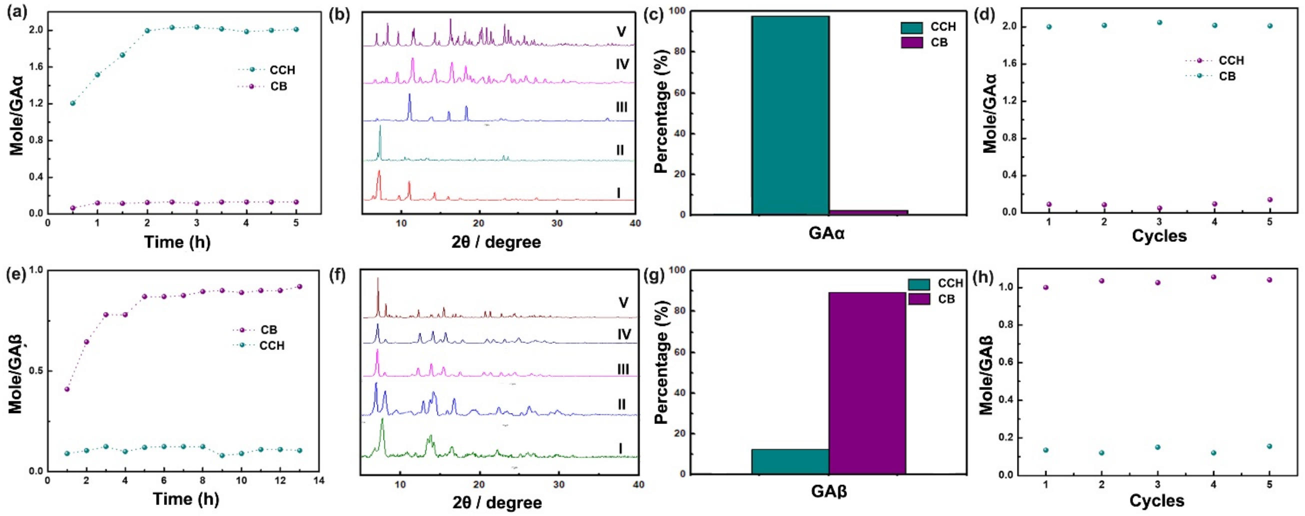


Figure 3. (a) Time-dependent **GAα** solid–liquid sorption plot for **CCH/CB** mixture solution at room temperature. Any surface adsorbed **CCH/CB** molecules and unstably complexed **CCH** molecules were removed by heating the absorbed crystal samples at 30 °C for 20 min. (b) PXRD patterns of **GA**: (I) original **GAα**; after adsorption of **CCH/CB** mixture solution for (II) 1 h, (III) 3 h, and (IV) 5 h; (V) simulated PXRD pattern from single-crystal structure of 4(**CCH**)⊂**GA**. (c) Relative amounts of **CCH** and **CB** adsorbed in **GAα** after 5 hours by gas chromatography. (d) Maximum uptake amount of **CCH** and **CB** in **GAα** after the same material is recycled five times. (e) Time-dependent **GAβ** solid–vapor sorption plot for **CCH/CB** mixture vapor at room temperature. Any surface adsorbed **CCH/CB** molecules were removed by heating the absorbed crystal samples at 30°C for 20 min. (f) PXRD patterns of **GA**: (I) original **GAβ**; (II) after adsorption of **CCH** vapor; (III) after adsorption of **CB** vapor; (IV) after adsorption of **CCH/CB** mixture vapor; (V) simulated PXRD pattern from single-crystal structure of **CB**⊂**GA**. (g) Relative amounts of **CCH** and **CB** adsorbed in **GAβ** after 13 hours by gas chromatography. (h) Maximum uptake amounts of **CCH** and **CB** in **GAβ** after the same material is recycled five times.

CB/CCH separation by GAα. Owing to the outstanding solid-state host–guest properties of **GA**, we envisioned that **GAα** possesses the capability of discriminating and selectively separating/absorbing **CB**/**CCH** mixture (1:1 v/v was always used) as aforementioned. Activated guest-free **GAα** crystals could be obtained by desolvating the host–guest binding crystals of 2(DCM)⊂**GA** (Scheme 1b-c, Figures S15-S16), which was grown by evaporation of a CH_2Cl_2/CH_3OH solution of **GA** (see Supporting Information), and the powder X-ray diffraction (PXRD) pattern of the activated crystalline solids was fully in line with the simulated PXRD pattern of the guest-free **GAα** crystals, hence, the structure of the desolvated crystalline phase was proved (Figure S17).

Due to the densely-packed arrangement of **GAα**, hardly any **CB** or **CCH** molecules can penetrate into the crystalloids by solid-vapor sorption (Figures S18), not to mention the induce of a selective loading process in a relative short time, thus, the solid-liquid direct contact adsorption process should be considered in priority. ^{1}H NMR experiments revealed that **GAα** preferred to absorb **CCH** upon immersing in a solution of **CB**/**CCH** mixture, and a high saturated uptake of **CCH** can be identified as nearly four Mole/**GA** (Figure S19), on the contrary, trace amount of **CB** can be absorbed. Surprisingly, gas chromatography (GC) experiment showed that the purity of **CCH** absorbed in **GAα** was 97.2% (Figure S20), proving the high selectivity of **CCH** in **GAα**. To be more confirmative, the single crystal structure of **CCH**-loaded **GAα** was obtained (see Supporting Information), in line with the adsorption test, **CCH** forms a 1:4 host–guest binding system with **GA** (referred to as 4(**CCH**)⊂**GA**, Scheme 1d, left). In this crystal structure, ladder-shaped **GA** molecules help form a sandwich packing mode with infinite extrinsic 2D diagonal channels, two rows of **CCH** molecules accommodated in each interlayer, malposed and stabilized by C-H···Cl interactions (Scheme 1d, right). Additionally, time-dependent PXRD pattern presents a continuous crystal-to-crystal transformation from **GAα** to 4(**CCH**)⊂**GA** over 5 hours (Figure 3b), further confirming that the mechanism of the selective adsorption is indeed a phase transformation process induced by preferable guests, and as for **GAα**, the winner is **CCH**.

In order to obtain **CCH** with a higher purity, any **CB** or **CCH** molecules attached to the surface of the crystalloids should be removed. Interestingly, after heating the adsorbed **GAα** (4(**CCH**)⊂**GA**) at 30 °C for 20 min, a stable intermediate state crystalline phase, where **CCH** forms a 1:2 host–guest complex with **GA** was obtained (referred to as 2(**CCH**)⊂**GA**, Scheme 1e, Figure S21), and then **CCH** could be released from 2(**CCH**)⊂**GA** with a purity about 98.0% (Figures 3c, S22). The stability of the two crystalline phases were verified by TG experiments, and compared to the release temperature of 4(**CCH**)⊂**GA** below 50 °C (Figure S23), hardly any weight loss of 2(**CCH**)⊂**GA** was seen until the crystals were heated to 90 °C (Figure S24). Overall, due to the relatively weak host–guest interactions and extremely high separation ratio, at least half of the **CCH** molecules could be facilely released from the 4(**CCH**)⊂**GA** crystals, endowing **GAα** with great potentials for practical use. What's more, aiming to obtain the most stable data representation, time-dependent solid-liquid sorption experiment by using **GAα** was carried out (Figures 3a, S25). The uptake of **CCH** increased rapidly in a form of nearly constant speed before reaching its saturation point (ca. 2h), and negligible amount of **CB** was uptaken in the experiment. Besides, the removal of the guest-loaded crystals, that is, 4(**CCH**)⊂**GA** and 2(**CCH**)⊂**GA**, could lead to the recovery of the original guest-free **GAα** phase (Figures S26-S28), which can be further reused at least 5 times without decreasing its **CCH** capture performance (Figure 3d), confirming the high selectivity/efficiency/recyclability of **GAα** as a new solid material for adsorption and separation.

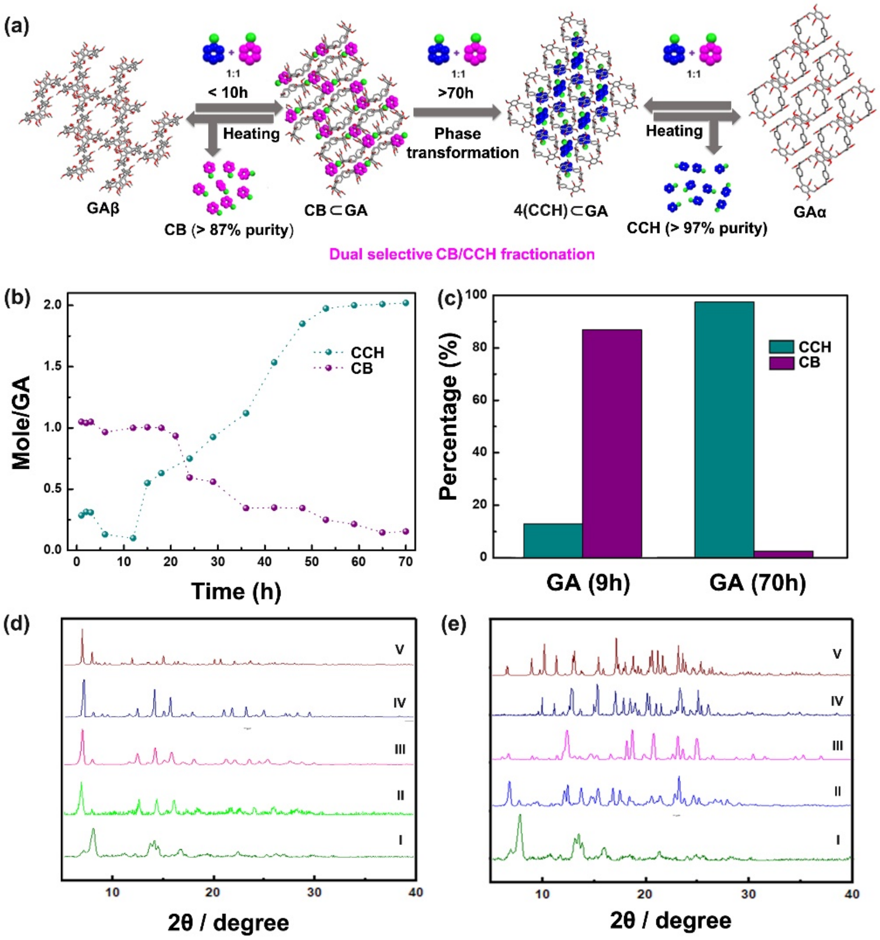


Figure 4. (a) Representation of the dual selective **CB**/**CCH** fractionation by immersing activated crystals of **GA** in **CCH**/**CB** mixture solution at room temperature. (b) Time-dependent **GAβ** solid–liquid sorption plot for **CCH**/**CB** mixture solution at room temperature. (c) Relative amount of **CCH** and **CB** adsorbed in **GAβ** before (9 h, left) and after (70 h, right) the crystalline phase transformation from **CB⊂GA** to 4(**CCH**)⊂**GA** by gas chromatography. (d) PXRD patterns of **GA**: (I) original **GAβ**; after adsorption of **CCH**/**CB** mixture solution for (II) 3 h and (III) 6 h; (IV) PXRD patterns of **CB⊂GA**; (V) simulated PXRD pattern from single-crystal structure of **CB⊂GA**. (e) PXRD patterns of **GA**: (I) original **GAβ**; after adsorption of **CCH**/**CB** mixture solution for (II) 24 h, (III) 48 h and (IV) 65 h; (V) simulated PXRD pattern from single-crystal structure of 4(**CCH**)⊂**GA**.

CB/CCH separation by GAβ. Active **GAβ** could be obtained by desolvating the **GAβ** crystals (Scheme 1g, Figures S29-30), which was initially recrystallized from toluene solution (see Supporting Information). As aforementioned, **GAβ** crystals possess a relatively sparse packing mode (Figure 1c, right), and its intrinsic pores prompted us to explore whether **GAβ** could discriminate the mixture of **CB** and **CCH** through direct solid-vapor adsorption. Thus, time-dependent solid-vapor sorption experiment by using **GAβ** was carried out (Figures 3e, S31). Interestingly, the selectivity of **GAβ** toward **CB**/**CCH** mixture was directly opposed to **GAα**, that is, the preferable guest is **CB** instead of **CCH** in terms of **GAβ** crystals. Similarly to the solid-liquid adsorption process by **GAα**, it took only about five hours to complete the whole separation and adsorption process, and a small amount of **CCH** was captured and proved very stable during the whole experiment (Figure 3e). GC experiments also confirmed a satisfactory selectivity for **CB** that is 88.2 % (Figures 3g, S32), meanwhile, PXRD pattern of **GAβ** phase transformed after adsorption indicated that a new crystalline phase with **CB**-loaded was generated (Figure 3f).

To rationalize this, we successfully obtained the single crystal structure of **CB⊂GA** by slow evaporation of CB/CH$_3$OH solution of **GA** (Scheme. 1g). In consistency with the ^{1}H NMR and TG experiments (Figures S33-S34), **CB** forms a 1:1 host–guest complex with **GA**, and many disordered CH$_3$OH molecules intracrystalline unable to be exactly refined were further determined by ^{1}H NMR, TGA and DSC experiments (Figures S35-S37). The PXRD pattern of **GAβ** after adsorption of the **CB**/**CCH** mixture vapor matched well with the pattern after adsorption of the **CB** vapor, also in a good agreement with the simulated profile from the single crystal structure of **CB⊂GA** (Figure 3f), which further confirming the process of adsorption and separation is in fact the guest-triggered crystalline phase transformation, in coordination with the relative stability of the new formed crystal structure upon complexation. In addition, it is worth mentioning that **GAβ** crystal with infinite 1D channels is not as stable as the dense-packed **GAα,** and the partial intrinsic pores could be collapsed during heating or desolvating process (Figure S38).[18] However, it still possesses the ability in discriminating and separating the mixture vapor of **CB**/**CCH** at least 5 times without losing its performance (Figure 3h).

Dual selective CB/CCH fractionation by GA. According to the two completely opposite selectivity of **GAα** and **GAβ**, we wonder if we can realize the uptake of the two compounds through only one special adsorption process, that is, fractionation of the **CB**/**CCH** mixture. Therefore, time-dependent solid-liquid sorption experiments using **GAβ** crystals were carried out (Figures 4b, S39-S41). As expected, due to the intrinsic porosity along the a-axis, a high-speed adsorption of **CB** and **CCH** with no obvious selectivity was observed instantaneously, soon afterwards, the intra-crystalline **CCH** molecules were gradually squeezed out to a minimum extend within about 10 hours. Intriguingly, the uptake amount of **CCH** began to increase rapidly after this point, and the original dominated **CB** molecules began to decrease and displaced by **CCH**. Time-dependent PXRD patterns indicated a guest-induced continuous crystalline phase transition from **CB⊂GA** to 4(**CCH**)⊂**GA**, following after **GAβ** to **CB⊂GA**, and the whole process was completed within about 65 hours (Figures 4d-e). Thus, a continuous and coherent process, that is, **CB** molecules in the **CB**/**CCH** mixture penetrate the **GA** crystals and induced the **CB⊂GA** formed firstly, soon afterwards, **CCH** molecules trigger the configuration conversion of the **GA** in **CB⊂GA** with the recovery of the binding ability toward **CCH** in solution, leading to the new phase of 4(**CCH**)⊂**GA** generated (Figure 4a). This suggests that the **CCH**-loaded 4(**CCH**)⊂**GA** is more thermodynamically stable than **CB**-loaded **CB⊂GA** and unloaded **GAβ** crystals.

Due to the successive phase transformation along with the loading and displacing one after another, molecular scale dual selectivity for **CB**/**CCH** separation can be obtained by **GA** molecular crystals. Two GC experiments confirmed that the fractionation of **CB** before the phase transformation is over 87% (Figure 4c, left, Figure S42), and the fractionation of **CCH** after completely phase transformation is over 97% (Figure 4c, right, Figure S43), which are all consistent with the results of solid-liquid or solid-gas separation by **GAα** and **GAβ** crystals as aforementioned. In other words, the **CB**/**CCH** fractionation process was a result of the opposite selectivity of the two **GA** crystals, in conjunction with the guest-induced configuration conversion and phase transformations, thus, the two mixed components could be separated orderly and effectively.

CONCLUSIONS

In conclusion, we presented an entirely new kind of macrocyclic arene, namely **GA**, which was designated according to its two totally different, but, indeed interconvertible molecular configurations. Taking advantage of its unique structural feature, lipophilic or hydrophilic species different in size, shape, and polarity could be hosted to form 1:1, 1:2 or 1:4 solid-state host–guest assemblies. In particular, **GA** presented a good binding affinity toward persistent environmental contaminant and Group 2B carcinogen 1,4-dioxane in the solid states, which displayed a nearly 80 °C boiling point elevation and resistance to weathering erosion over 1000 hours. Most importantly, we have investigated the **CB**/**CCH** separation by **GA**-base crystalloids of **GAα** and **GAβ**. **CCH** can be highly purified by **GAα** from an **CB**/**CCH** mixture solution through solid-liquid sorption with purity over 97%, and **GAβ** has the ability to separate **CB** from the **CB**/**CCH** mixture vapor through solid-vapor sorption with purity of over 88%, and both of them can be reused many times without decrease in separation performance. Furthermore, we demonstrated that **GAβ** and the two guest-loaded crystals (**CB⊂GA** and 4(**CCH**)⊂**GA**) could be transformed one after another by continuous guest-induced operation. Hence, **CB** and **CCH** could be separated consecutively in different stages of crystalline phase over time, as a form of fractional distillation process, and the dual selectivity for the separation of **CB**/**CCH** mixture by one special macrocycle-based crystals could be achieved.

Above all, compared with other macrocycle-based crystalline separation materials, such as pillarenes, **GA** has several advantages. Firstly, an efficient high yield fragment coupling process makes **GA** can be prepared easily and full of potentials for mass production upon fine-tuning of the synthetic details and separation approaches. Secondly, up to 1:4 unusual host–guest binding forms will bring **GA** with a relatively high overall guest uptake. Thirdly, multiple crystalline phases transformed in order by guest-inducement in solution endows **GA** with dual selectivity in adsorption and separation of **CB**/**CCH** mixture in only one cycle of operation. We strongly believe that dual or multiple separation selectivity will be one of the future development directions of synthetic macrocycles-based crystalline separation materials. Discovery of triple selective separation system based on **GA** and/or other novel synthetic macrocycles is still ongoing in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
Chemical synthesis and characterization; Crystal structure analysis; TG, DSC, PXRD and GC analysis; Crystallographic data for **GAα** (CIF/1903737), **GAβ**(CIF/1903739), 2(DCM)⊂**GA** (CIF/1852587), 1,4-dioxane⊂**GA** (CIF/1903700), 4(1,3-dioxane)⊂**GA** (CIF/1903732), 4(THP)⊂**GA** (CIF/1903735), 2(DEM)⊂**GA** (CIF/1903730), 4(**CCH**)⊂**GA** (CIF/1903734), **CB⊂GA** (CIF/1903736), and all experimental details (PDF).

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Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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