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CD-MOF: A Versatile Separation Medium

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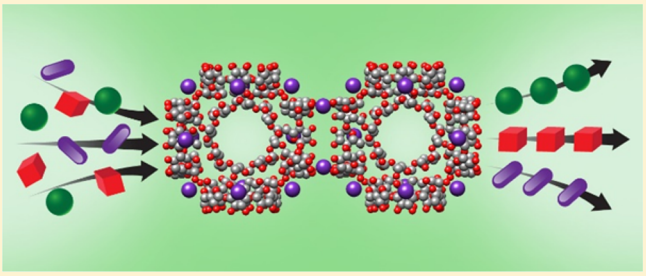
Supporting Information

ABSTRACT: Porous metal−organic frameworks (MOFs) have been studied in the context of a wide variety of applications, particularly in relation to molecular storage and separation sciences. Recently, we reported a green, renewable framework material composed of γ-cyclodextrin (γ-CD) and alkali metal salts—namely, CD-MOF. This porous material has been shown to facilitate the separation of mixtures of alkylaromatic compounds, including the BTEX mixture (benzene, toluene, ethylbenzene, and the regioisomers of xylene), into their pure components, in both the liquid and gas phases, in an energy-efficient manner which could have implications for the petrochemical industry. Here, we report the ability of CD-MOF to separate a wide variety of mixtures, including ethylbenzene from styrene, haloaromatics, terpinenes, pinenes and other chiral compounds. CD-MOF retains saturated compounds to a greater extent than their unsaturated analogues. Also, the location of a double bond within a molecule influences its retention within the extended framework, as revealed in the case of the structural isomers of pinene and terpinine, where the isomers with exocyclic double bonds are more highly retained than those with endocyclic double bonds. The ability of CD-MOF to separate various mono- and disubstituted haloaromatic compounds appears to be controlled by both the size of the halogen substituents and the strength of the noncovalent bonding interactions between the analyte and the framework, an observation which has been confirmed by molecular simulations. Since CD-MOF is a homochiral framework, it is also able to resolve the enantiomers of chiral analytes, including those of limonene and 1-phenylethanol. These findings could lead to cheaper and easier-to-prepare stationary phases for HPLC separations when compared with other chiral stationary phases, such as CD-bonded silica particles.



INTRODUCTION

Purification of chemical commodities is a cornerstone of modern chemistry on both the laboratory and industrial scales. Although improvements to the efficiency and cost-effectiveness of purifications have traditionally been major goals in an industrial context, recently there has been a significant push toward minimizing the impact of chemical processes on the environment, leading to the rise of an entirely new branch of chemistry—namely, green chemistry.[1] Porous materials, such as zeolites,[2] have been used for several decades in the industrial-scale processing of petrochemicals,[3] particularly in catalytic transformations of aromatic hydrocarbons, including disproportionations,[4] (trans)alkylations, and isomerizations.[5] In addition, zeolite-based adsorbents are often used to separate the products from these reactions.[6]

The advent of porous coordination polymers, pioneered by Robson,[7] revolutionized the field of porous materials, which, up until his seminal investigations had been mostly focused on inorganic zeolites and activated carbons. Subsequently, the approach of linking well-defined organic struts with transition metal cations has led to the formation[8] of a plethora of new porous materials with unique and tunable properties. These materials—more commonly referred to as metal−organic frameworks (MOFs)[9]—have been shown to have applications in (i) gas storage,[10] with particular emphasis placed on their ability to store H_2;[10b,11] (ii) carbon capture and sequestration;[10e,12] (iii) catalysis;[13] and (iv) separation science.[13b,14]

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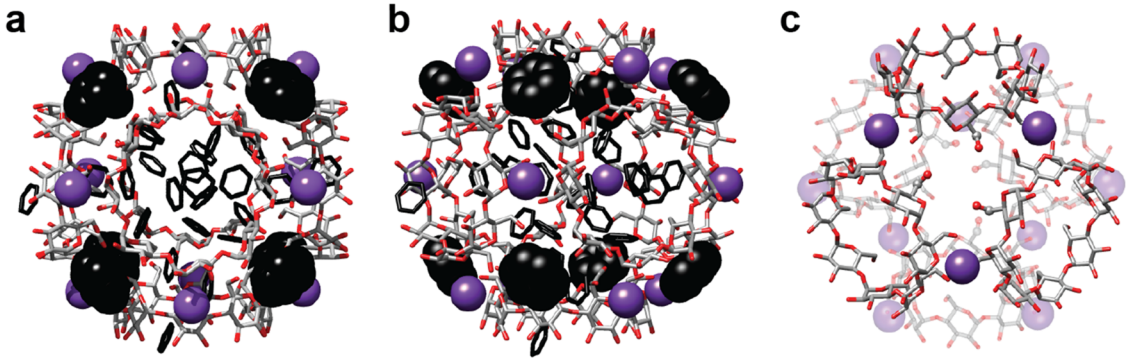

Figure 1. Grand canonical Monte Carlo (GCMC) simulations of benzene within CD-MOF-2 determined at 1 kPa. (a,b) Representations of a $(\gamma\text{-CD})_6$ cube portion of CD-MOF that show benzene residing in the large 1.7 nm diameter pore (center of image) and in the transverse pores located between adjacent $(\gamma\text{-CD})_6$ cubes (stick representations, black), as well as a single benzene molecule located in each of the eight triangular-shaped pores (space-filling representations, black). (c) View of the triangular-shaped pore along the ⟨111⟩ direction, revealing the presence of free primary hydroxyl groups (ball-and-stick representation) that may act as sites to hydrogen bond with molecules of methanol from the crystallization procedure, which could effectively block the entrance of this pore and prevent passage of benzene and toluene, limiting their retention within the framework.

The ability to alter the size and shape of the pores within MOFs has led to these architectures being used as shape-selective materials that preferentially retain compounds with specific dimensions, a particularly useful property during the separation of constitutional isomers of xylene, hexane and other hydrocarbons.[14f,15] Chiral porous frameworks have also been prepared and shown (i) to resolve enantiomers[16] and (ii) to find application in the area of asymmetric catalysis.[17]

Recently, we have reported[18] the synthesis and characterization of CD-MOF, a green, renewable, porous framework constructed from γ-cyclodextrin (γ-CD) and alkali metal salts.[19] CD-MOF can be prepared entirely from food-grade precursors[20] and is able to sequester large quantities of CO_2[21] as well as facilitate the separation of a variety of alkylaromatic compounds under analytical HPLC conditions at ambient temperature.[22] Most importantly, for potential industrial applications, both CD-MOF-1 and CD-MOF-2 are able to separate BTEX mixtures (benzene, toluene, ethylbenzene, and the regioisomers of xylene) with high selectivity and a retention order of *ortho-* > *meta-* > *para*-xylene.[23] This retention order is also observed for the separation of regioisomers of other alkylaromatic substances, including ethyltoluene and cymene.[22] Additionally, a report of a zeolitic material (i) with a solid-state structure analogous to those of CD-MOF-1, -2, and -3, and (ii) with pores of a similar size and which also display the ability to separate regioisomers of alkylaromatic compounds with the same retention order of the regioisomers, has recently appeared in the literature.[24]

In this paper, we describe the application and versatility of CD-MOF-1 and CD-MOF-2 toward the separation of a range of organic compounds, including (i) saturated and unsaturated aromatic and alicyclic, (ii) chiral, and (iii) haloaromatic compounds. To date, very few MOFs reported in the literature have been shown to separate a wide variety of different compounds.[25] A key component of CD-MOFs is the large number of free hydroxyl groups which are easily accessible. These hydroxyl groups have been shown to react with epoxides to create cross-linked CD-MOFs which can form amorphous gels in aqueous media.[19a] They also play a key role in the large, reversible uptake of CO_2 within the CD-MOF extended framework.[21] Chemisorption is the main process through which CO_2 is trapped at low pressure as a consequence of the formation of carbonate functions at the free primary hydroxyl groups, which are also available to interact noncovalently with guest molecules within the extended framework of CD-MOFs. Another source of the versatility in CD-MOFs is the chirality (40 stereogenic centers!) associated with each γ-CD torus. The chirality of γ-CD is maintained throughout the extended structure of CD-MOF, affording a homochiral framework capable of enantiomeric recognition and the separation of racemic mixtures.

EXPERIMENTAL SECTION

Details of the CD-MOF preparation, HPLC column packing, and HPLC separation conditions have been reported previously.[22] Briefly, CD-MOF-1 was prepared by a bottom-up approach, wherein the MOF was grown in the presence of CTAB in order to restrict the crystallite size to 10−15 μm. These particles were then slurry-loaded into a 250 × 4.6 mm analytical HPLC column using hexane as the mobile phase. Unless otherwise stated, all separation experiments were carried out at ambient temperature at a flow rate of 1 mL/min using HPLC-grade hexane as the mobile phase.

RESULTS AND DISCUSSION

Separation of Benzene and Toluene. In a previous paper,[22] we reported the observation that, with continued washing with hexane, the retention times of benzene and toluene shift to longer times (approximately an additional 12 and 40 min for toluene and benzene, respectively), while the retention times of larger molecules, such as the regioisomers of xylene, remain unchanged, indicating that both CD-MOF-1 and CD-MOF-2 can be activated in order to achieve favorable retention of benzene and toluene. Furthermore, this activation process is reversible, insofar as washing the CD-MOF column with an alcohol/hexane mixture results in a decrease in retention time very similar to that obtained with a freshly prepared column, while subsequent washings with CH_2Cl_2 reactivates the column. This observation suggested that there are sites within CD-MOFs that are ideal for the retention of benzene and toluene, yet are too small for retention of larger molecules, that can be blocked by the presence of an alcohol such as methanol which can be removed readily by washing with CH_2Cl_2. As a consequence of the disordered nature of the solvent molecules within the solid-state structure of CD-MOFs, the location of benzene or toluene within activated CD-MOF

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cannot be observed directly. To help understand our previous observations, we performed grand canonical Monte Carlo (GCMC) simulations to determine the locations within CD-MOFs that can be occupied by benzene and toluene. GCMC simulations on CD-MOF-2, calculated at the saturation capacity of 1 kPa, show that benzene and toluene can occupy the small triangular pores between $(\gamma\text{-CD})_6$ cubes (Figure 1). These pores have triangular openings, the size of which is ~5.1 Å, determined by geometric pore-size distribution calculations (see Figure S7), while benzene and toluene have kinetic diameters of ~5.8 Å. Although benzene and toluene are larger than the openings of the triangular pores, a previous investigation on silicalite revealed that benzene can be adsorbed by this porous material, even though it is of a size that exceeds the nominal pore dimensions.[26] Additionally, it is possible that the hydroxyl groups lining the opening of the pores can rotate and allow benzene and toluene molecules to pass through. When we compare the GCMC simulations for toluene and benzene with those obtained for xylene isomers (see Figure S8) and reported in our previous publication,[22] it transpires that none of the xylene isomers can be adsorbed in these small pores as a result of their larger kinetic diameters.

Separation of Saturated, Unsaturated, and Chiral Aromatic and Alicyclic Compounds. In order to test the versatility of CD-MOFs as stationary phases for HPLC, the separations of a range of compounds were put to the test using this framework. Of particular interest is the separation of ethylbenzene from styrene since the latter is an important chemical commodity in the production of polymeric materials.[27] Styrene is typically produced by the catalytic dehydrogenation of ethylbenzene,[28] affording a product which often contains a large amount of unreacted ethylbenzene.[29] As a consequence of the reactivity of the vinyl group in styrene,[29] together with the very similar boiling points of ethylbenzene (409 K) and styrene (418 K), conventional distillation is impractical on an industrial scale.[30] Additionally, the presence of inhibitors or the use of low pressures is required in order to prevent polymerization of styrene. Research into the separation of these compounds by exploiting differences in adsorptivity to porous materials has been intense of late, with a number of MOFs,[29] such as MIL-47,[14b,f] MIL-53,[14f,31] HKUST-1,[32] and MIL-101,[15c] having all been demonstrated to separate ethylbenzene and styrene. Despite the fact that this separation is well-researched, the advantage of CD-MOF, in comparison with these MOFs, is that its preparation is environmentally benign.[18a]

Upon injection (10 μL) of a 50 mg/mL mixture of ethylbenzene and styrene in hexanes onto a CD-MOF-1 column, using hexane as the mobile phase, baseline separations of ethylbenzene and styrene were achieved (Figure 2), with ethylbenzene eluting from the column (9.6 min) before styrene (14.3 min), giving a separation factor (α) of 1.75.[33] Although HKUST-1 (MOF-199)[32] has also been shown to be highly effective in the separation of ethylbenzene and styrene, with retention times of 35 and 125 min, respectively, using identical conditions (250 × 4.6 mm, hexane, 1 mL/min) to those reported here, in this particular instance, the separation is believed to be a consequence of π-complexation of styrene with the copper sites within the stationary phase, rather than separation resulting from size or shape selectivity.

Quantum mechanical calculations (see Figure S11) were employed to investigate the binding energies of ethylbenzene and styrene with an isolated γ-CD ring, the major structural

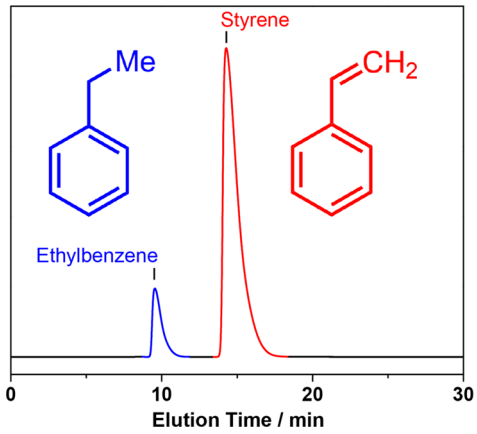

Figure 2. Liquid-phase HPLC traces illustrating the separation of ethylbenzene (blue) and styrene (red) using CD-MOF-1 (particle size 10−15 μm) as the stationary phase, column dimensions 250 × 4.6 mm, using HPLC-grade hexane as the mobile phase at a flow rate of 1 mL min^{-1} at 298 K, monitored at a wavelength of 266 nm.

component of the CD-MOFs. It was found that styrene (−79 kJ/mol) interacts more favorably as compared to ethylbenzene (−57 kJ/mol). The optimized binding geometries of the guests within the γ-CD ring are very different: ethylbenzene prefers to adopt a relative orientation such that its aromatic ring lies almost perpendicular to the C_8 axis of γ-CD, whereas styrene prefers to orient itself almost parallel to the C_8 axis and closer to the inner wall of the γ-CD ring. The large difference in binding energies suggests that a significant component that contributes toward the ability of CD-MOF-1 to separate ethylbenzene and styrene is the more favorable interactions between styrene and the macrocyclic components of the extended framework.

The separations of other saturated and unsaturated aromatic compounds were also investigated—specifically the separations of (i) cumene from α-methylstyrene and (ii) 4-ethyltoluene from 4-methylstyrene. α-Methylstyrene is produced from cumene and it is also a coproduct in the production of phenol from cumene.[34] The separation factors for these compounds employing CD-MOF-1 are shown in Tables S2 and S3. In the case of the separation of the methylstyrenes, we observe that the *para*-isomer is eluted faster than the *meta*-isomer, which is the same order of elution that is observed for the regioisomers of ethyltoluene.

Alicyclic compounds which exist as constitutional isomers, consequent upon the positioning of a double bond, were also considered as potential candidates to be separated by CD-MOFs. The terpinenes can exist in one of four constitutional isomers: α-, β-, γ-, and δ-terpinene (Figure 3). The α- and γ-terpinenes possess an endocyclic double bond, while β- and δ-terpinene have exocyclic double bonds. Upon comparison of the chromatograms (Figure 3a) of α-, γ-, and δ-terpinene, it can be seen that, although the two isomers with endocyclic double bonds cannot be separated by the CD-MOF-1 stationary phase, δ-terpinene with its exocyclic double bond is retained much longer on the column and hence could be readily separated from the α- and γ-isomers. *p*-Cymene elutes at a similar time to α- and γ-terpinene, indicating that the presence of a benzenoid ring has little impact on retention time.

The pinenes constitute another set of alicyclic compounds with isomers that possess either an endocyclic (α-pinene) or exocyclic (β-pinene) double bond. In addition to these

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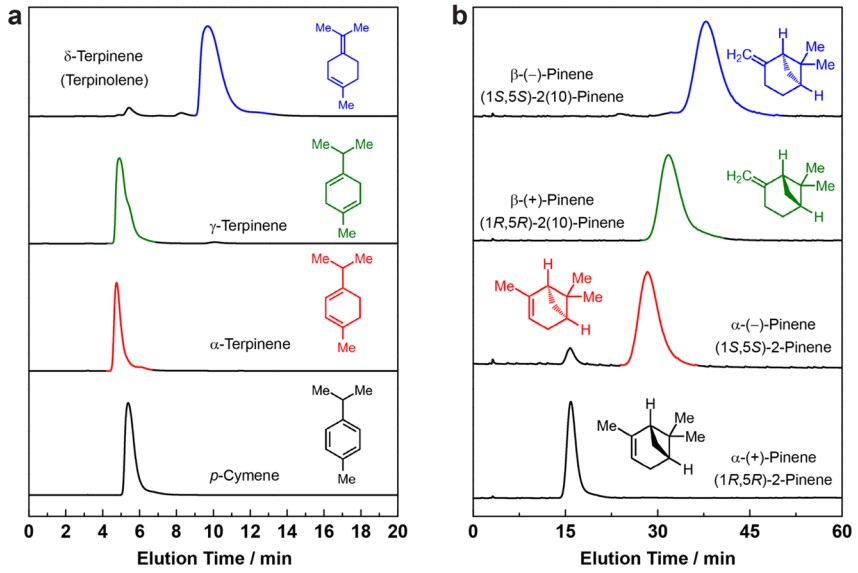

Figure 3. Liquid-phase HPLC traces illustrating the difference in retention of (a) terpinene isomers and the aromatic analogue *p*-cymene, monitored at a wavelength of 212−220 nm and (b) pinene isomers, monitored at a wavelength of 210 nm using CD-MOF-1 (particle size 10−15 μm) as the stationary phase, column dimensions 250 × 4.6 mm, using HPLC-grade hexane as the mobile phase at a flow rate of 1 mL min^{-1} at 298 K. The small black peaks represent the detection of impurities.

constitutional isomers, each regioisomer is chiral as a consequence of the stereogenic centers located at the 1 and 5 positions on the carbon skeleton, resulting in pinene having a total of four isomers. Chromatograms of each of these isomers (Figure 3, Table 1) reveal that, as was observed in the case of the terpinenes, the isomers with the exocyclic double bond are retained by CD-MOF-1 for a longer period of time than the isomers possessing an endocyclic double bond. In addition to separations based on the location of the double bonds, the enantiomers of both α- and β-pinene can be resolved. This example of *chiral* separation is by no means unique, with the enantiomers of limonene and 1-phenylethanol also being completely resolved by CD-MOF-1 (see the Supporting Information). The selectivity factor of (*R*)-(+)-limonene over its enantiomer is 1.72, while the selectivity factor of (*S*)-(−)-1-phenylethanol over its mirror-image counterpart is 2.26. The separation of the 1-phenylethanol enantiomers using CD-MOF-1 is superior to that reported using a chiral-modified UMCM-1 MOF as a stationary phase.[16a] The ability of CD-MOF-1 to separate enantiomers is not surprising, given that it is a homochiral extended framework as a consequence of the 40 stereogenic centers present in each γ-CD torus.[35] A racemic mixture of 1-phenylethanol requires the use of a more polar mobile phase (CH_2Cl_2) in order for it to be eluted from the column, presumably because of the strong hydrogen bonding interactions between the framework and 1-phenylethanol. This result demonstrates that, not only does separation take place as a consequence of shape and stereo selectivity, but the ability of the analyte to hydrogen bond with CD-MOF-1 must also be considered. Although the cavity within γ-CD, through which compounds must travel in order for separation to take place, is relatively hydrophobic,[36] the oxygen atoms linking the D-glucopyranosyl units within the cyclic structure, as well as the free primary hydroxyl groups, can potentially interact with polar compounds. We conclude that CD-MOF-1 can serve as a stationary phase material for normal-phase separations.

Table 1. CD-MOF-1 Column Separation Factors Calculated from Single-Component Measurements of Pinene Using *n*-Hexane as the Mobile Phase at a Flow Rate of 1 mL min^{-1}

	α-(+)-pinene	α-(−)-pinene	β-(+)-pinene	β-(−)-pinene
α-(+)-pinene	–	0.50	0.44	0.36
α-(−)-pinene	1.99	–	0.88	0.72
β-(+)-pinene	2.27	1.14	–	0.83
β-(−)-pinene	2.76	1.38	1.21	–

Separation of Haloaromatic Compounds. The propensity of CD-MOF-1 to act as a versatile stationary-phase separation medium is also highlighted by the variation in retention times exhibited by a number of aromatic compounds that have been substituted with one or two halogen atoms. Benzene and fluorobenzene have very similar sizes (effective van der Waals radii H = 120 and F = 147 pm),[37] and so it would be expected that their interaction with CD-MOF-1, based on size and shape alone, would be close to identical. Chromatograms of the pure compounds, however, using hexane as the mobile phase (Figure 4), show that fluorobenzene is much more strongly retained than benzene within the CD-MOF-1 stationary phase, with an approximately 90-min difference in retention time observed under these HPLC conditions (see Table 2 for separation factors based on single-component measurements). We speculate that a possible reason for the stronger retention of fluorobenzene over benzene is a result of C−H···F and C−OH···F noncovalent bonding interactions that could occur between the framework and the molecules.[38] A similar comparison can be made between two other size-related molecules[37]—namely, bromobenzene (Br = 195 pm) and toluene (Me = 171−223 pm), where bromobenzene is retained on the CD-MOF-1 column an additional 40 min longer than toluene (see Figure S5). The observed order of retention for a monosubstituted benzenoid ring is F > Cl > Br > H > Me > I. It is likely that retention times are governed by both size/shape, as well as ability of the molecules to interact noncovalently with CD-MOF-1's extended framework.

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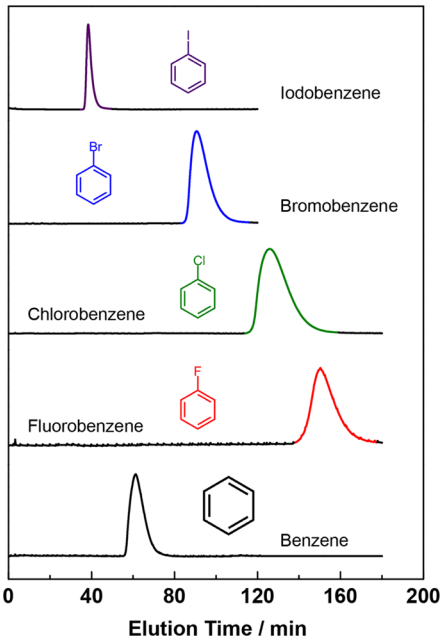

Figure 4. Liquid-phase HPLC traces illustrating the elution times of fluoro-, chloro-, bromo-, and iodobenzene compared to that of benzene using CD-MOF-1 (particle size 10−15 μm) as the stationary phase, column dimensions 250 × 4.6 mm, using HPLC-grade hexane as the mobile phase at a flow rate of 1 mL min^{-1} at 298 K, monitored at a wavelength of 212 nm (202 nm for fluorobenzene). A visible amount of noise is present at the wavelength used to detect fluorobenzene.

Table 2. CD-MOF-1 Column Separation Factors Calculated from Single-Component Measurements of Monohalogenated Aromatics Using *n*-Hexane as the Mobile Phase at a Flow Rate of 1 mL min^{-1}

	fluoro-benzene	chloro-benzene	bromo-benzene	iodo-benzene
fluorobenzene	–	1.19	1.68	4.2
chlorobenzene	0.84	–	1.40	3.50
bromobenzene	0.59	0.71	–	2.49
iodobenzene	0.23	0.28	0.40	–

Quantum mechanical calculations, carried out on a single γ-CD ring with a haloaromatic molecule, reveal a trend of binding interactions in direct contrast to the experimentally determined retention times. We performed geometry optimizations for an isolated γ-CD ring and calculated the binding energy for each haloaromatic compound (see Figure S12). Theory suggests that fluorobenzene interacts with γ-CD more weakly than do larger haloaromatic compounds, with affinities decreasing in the following order: I > Br > Cl > F = H. The calculated binding energies range from −38 kJ/mol for benzene and fluorobenzene to −53 kJ/mol for iodobenzene. These quantum mechanical calculations, however, do not support the experimental results. These findings suggest that the ability of this porous γ-CD architecture to separate haloaromatic compounds is an emergent property of CD-MOF,[39] rather than an intrinsic property of γ-CD. Although the interaction calculated between fluorobenzene and γ-CD is weaker than that between larger haloaromatic compounds, it is likely that the observed enhanced retention of fluorobenzene within CD-MOF is a consequence of entropic effects. The nature of the mobile phase (*n*-hexane) is also likely to influence the selectivity and retention of compounds separated using CD-MOF as a stationary phase. Eluent effects have been reported recently in the separation of the regioisomers of xylene using MIL-53(Al) as a stationary phase,[40] whereby the eluent influences both the adsorbent−adsorbate interactions and the adsorption capacity.

In contrast, GCMC simulations (Figure 5) of the adsorption of monohalogenated benzenes within CD-MOF at saturation pressure are found to be in general agreement with the experimentally determined HPLC results. These calculations show that the amount of monohalgenated benzene which can be adsorbed by the framework decreases in the order F > Cl > Br > I, suggesting that the smaller adsorbates are able to pack more efficiently within the extended porous framework. It should also be noted that iodobenzene is too large to fit within the small triangular pore that can accommodate the smaller monohalobenzenes. Comparison of the amount adsorbed between the similarly sized molecules benzene and fluorobenzene (see Table S9) reveals that an almost identical number of these molecules are taken up per unit cell of CD-MOF, yet this result still does not account for the large difference in retention

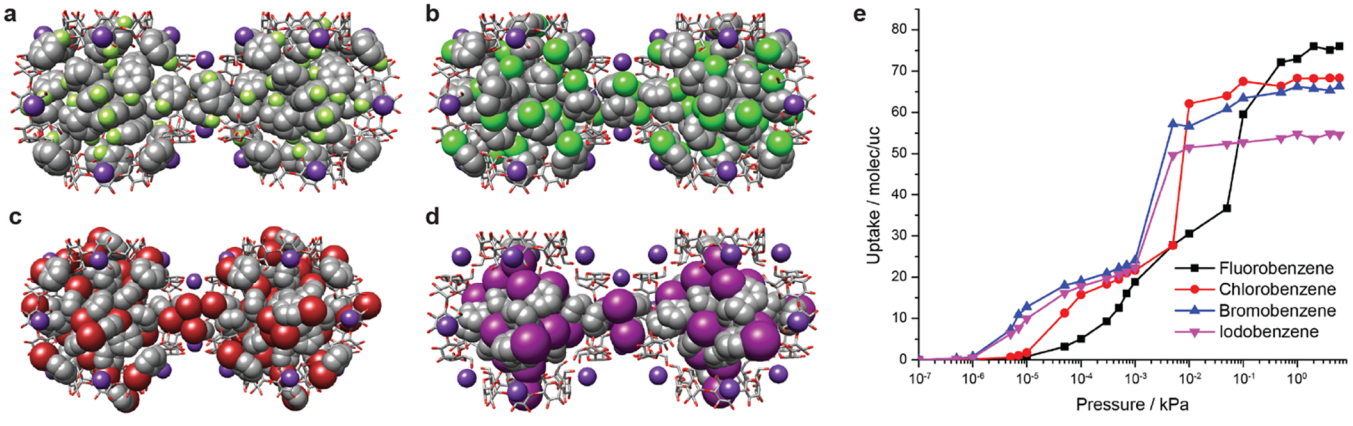

Figure 5. GCMC simulation snapshots at 6 kPa for (a) fluorobenzene, (b) chlorobenzene, (c) bromobenzene, and (d) iodobenzene. The haloaromatic molecules are represented as space-filling models, and the cross-section of CD-MOF-2 is represented as a stick model with F light green, Cl bold green, Br dark red, I purple, and Rb dark purple. (e) GCMC simulation isotherms at 298 K reveal the number of molecules of halobenzene per unit cell of CD-MOF over a wide range of pressure.

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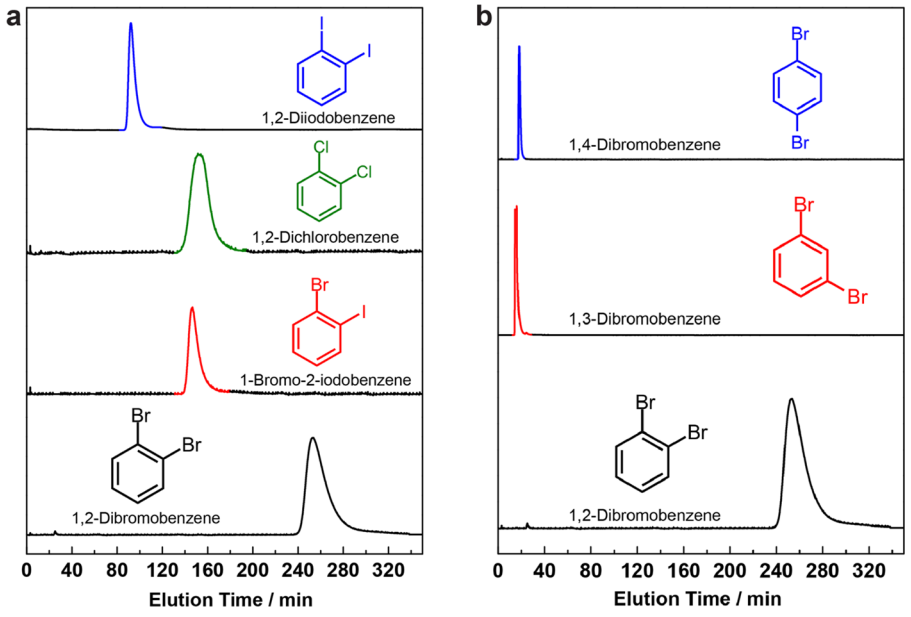

Figure 6. Liquid-phase HPLC traces illustrating the separations of (a) 1,2-dichloro-, 1,2-dibromo-, 1,2-bromoiodo-, and 1,2-diiodobenzene and (b) 1,2-, 1,3-, and 1,4-dibromobenzene, using CD-MOF-1 (particle size 10−15 μm) as the stationary phase, column dimensions 250 × 4.6 mm, using HPLC-grade hexane as the mobile phase at a flow rate of 1 mL min^{-1} at 298 K, monitored at a wavelength of 205 nm. A significant amount of noise is observed at this detection wavelength.

time between these two molecules which is observed in HPLC experiments. When a comparison of the adsorbate−adsorbate and adsorbate−adsorbent potential energies for benzene and fluorobenzene is made (see Table S11), the total energy for benzene adsorption is found to be −52 kJ/mol, which is less than that found for fluorobenzene (−57 kJ/mol). This suggests that even though a similar number of molecules of benzene and fluorobenzene can be adsorbed by CD-MOF, fluorobenzene can interact more favorably with the extended porous framework and it also takes part in more favorable adsorbate−adsorbate interactions within CD-MOF. Further analysis of the adsorption energies of chloro-, bromo-, and iodobenzene uptake within CD-MOF show that these compounds have more favorable interactions with the extended porous framework; however, entropic demands likely play an important role in determining selectivities for molecules of different sizes.

A very different result was obtained on examining dihaloaromatic compounds with respect to their monohalogenated counterparts. In common with dialkylated aromatic systems, the 1,2-disubstituted haloaromatic species were retained by CD-MOF-1 for the longest period of time; however, the order of elution of the 1,3- and 1,4-isomers is reversed compared with that for *m*- and *p*-xylene, with the 1,3-isomer eluting approximately 1−2 min before the 1,4-isomer in the case of dibromo- and bromoiodobenzene (Figure 6). This order of elution is identical to that described for the separation of the dichlorobenzene regioisomers using MIL-101(Cr).[15c] The most remarkable result, however, is the retention time of 1,2-dibromobenzene, which elutes after approximately 253 min using hexane as the mobile phase. In comparison with the other 1,2-dihalobenzene systems tested—including 1-bromo-2-iodobenzene, 1,2-dichlorobenzene and 1,2-diiodobenzene—1,2-dibromobenzene is retained for the longest period of time, i.e., almost 100 min longer than the respective dichlorobenzene and bromoiodobenzene, while 1,2-diiodobenzene is retained for the shortest period of time, eluting after 92 min (see Table 3 for separation factors based on single-component measurements). Given that the elution time of the 1,2-dihalobenzenes are significantly longer than those of their respective monohalobenzenes, it is possible that a bifurcated halogen bonding interaction between the dihalobenzene and CD-MOF-1 may be responsible for strong retention of the 1,2-dihaloaromatic compounds. The order of elution of these dihalobenzenes, however, cannot be explained by halogen bonding interactions alone. It might be expected that iodo substituents[41] would form the strongest halogen bonds with CD-MOF-1, most likely with a −C−O−C− group or a free primary or secondary hydroxyl group. This expectation is not reflected in the comparison of elution times of both the mono- and disubstituted haloaromatics, suggesting that the size of the aromatic compound and its ability to pack efficiently and adopt an optimal orientation for halogen bonding with the CD-MOF-1 framework is also a major determining factor in these systems, similar to that observed[22] in the case of the alkylaromatic separations.

Table 3. CD-MOF-1 Column Separation Factors Calculated from Single-Component Measurements of 1,2-Dihalogenated Aromatics Using *n*-Hexane as the Mobile Phase at a Flow Rate of 1 mL min^{-1}

	1,2-dichloro-benzene	1,2-dibromo-benzene	1,2-dibromo-iodobenzene	1,2-diiodo-benzene
1,2-dichlorobenzene	–	0.59	1.04	1.68
1,2-dibromobenzene	1.67	–	1.74	2.81
1,2-bromoiodobenzene	0.96	0.57	–	1.61
1,2-diiodobenzene	0.59	0.35	0.62	–

In order to gain a better understanding of the interaction between dibromobenzene and CD-MOF-1, we also calculated the binding energy for the 1,2-, 1,3-, and 1,4-dibromobenzene isomers. A comparison of the binding energies of the dibromobenzene isomers with the γ-CD ring is presented in Figure 7. Quantum mechanical calculations reveal that the

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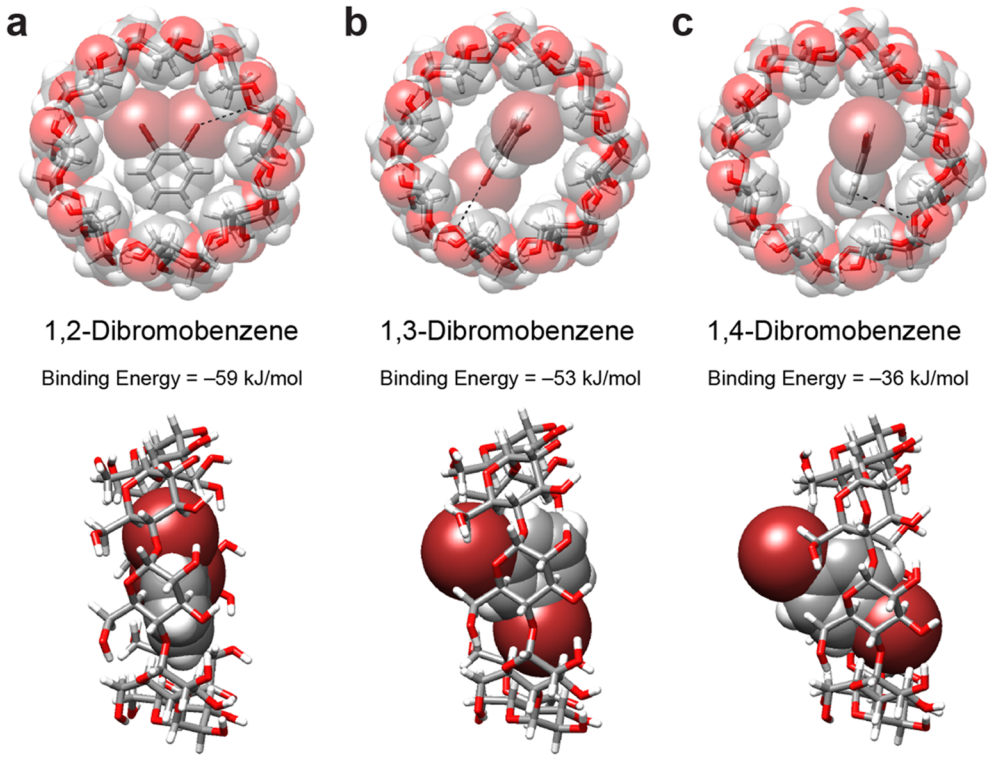

Figure 7. Quantum mechanical calculations of the optimal geometries for the interaction between γ-CD and (a) 1,2-, (b) 1,3-, and (c) 1,4-dibromobenzene optimized with the M06 functional and the 6-311g(d,p) basis set. Single-point calculations were performed using M06/6-311g(d,p) with counterpoise correction. Top images illustrate the view down the C_8 axis of γ-CD, with both the macrocycle and dibromobenzene represented by stick models with a transparent space-filling model overlay. Dashed lines between Br atoms (dark red) and O atoms (red) represent weak halogen bonding interactions. Bottom images show the side-on view with the γ-CD ring represented by a stick model and the dibromobenzene represented by a space-filling model.

interaction between the 1,2-isomer and γ-CD is the most favorable (−59 kJ/mol), closely followed by the 1,3-isomer (−53 kJ/mol), while the interaction of γ-CD with the 1,4-isomer is significantly less favorable (−36 kJ/mol). This observation is in good agreement with the HPLC experiments (Figure 6), where a significantly longer elution time is observed for 1,2-dibromobenzene. The preference for the 1,2-isomer in CD-MOF-1 is also in accord with a previous investigation,[22] where CD-MOF-1 was shown to be highly selective toward *ortho*-xylene in a mixture of xylene isomers. The optimized geometry suggests the presence of weak, noncovalent interactions between dibromobenzene and the glycosidic oxygen atoms of γ-CD for the 1,2-, 1,3-, and 1,4-isomers (Br···O distances of 3.50, 3.38, and 3.62 Å, respectively; see dashed lines in Figure 7). The major difference between the binding geometry of the 1,2-isomer within γ-CD and that for the other isomers arises from the fact that the 1,2-isomer lies almost perpendicular to the C_8 axis of γ-CD, whereas the remaining two isomers do not fit nearly as well within the γ-CD cavity, which may be expected to lead to less efficient packing of these two isomers within the CD-MOF-1 framework. GCMC simulations of the different regioisomers of dibromobenzene (see Table S11 and Figure S9), however, show that all the isomers have a very similar uptake within CD-MOF, with the 1,2-isomer adsorbing slightly more per unit cell than the 1,3- and 1,4-isomers, as well as very similar adsorbate−adsorbate and adsorbate−adsorbent interactions. It should be noted that the 1,2-isomer reaches its maximum adsorption to CD-MOF at a pressure (0.00001 kPa) half an order of magnitude lower than that for the other two isomers.

Quantum mechanical calculations of the interactions between γ-CD and the different 1,2-dihalobenzenes illustrated in Figure S13 show a binding interaction trend that is the reverse of the retention order that is observed experimentally. These calculations suggest that the interaction between 1,2-diiodobenzene and γ-CD is stronger than any of the other 1,2-dihaloaromatic compounds tested. Although quantum mechanical calculations appear to be able to determine accurately the preference for CD-MOF to retain 1,2-functionalized aromatic compounds, suggesting that the shape preference is defined by the shape of the γ-CD tori, size selection is defined by the extended porous framework and adsorbate−adsorbate interactions. The results from quantum mechanical calculations show that the versatile separation ability of CD-MOF is an emergent phenomenon,[39] and not a property of individual γ-CD tori acting on their own. GCMC simulations (see Table S10 and Figure S9) reveal that 1,2-dichlorobenzene has a higher adsorption uptake at saturation pressure than 1,2-dibromobenzene. However, upon examination of the simulation snapshots at saturation pressure, it is observed that 1,2-dichlorobenzene is occupying the small triangular pore. We are of the belief that 1,2-dichlorobenzene cannot access this pore since it approaches the size of *o*-xylene (which does not fit in this pore) and may be too large to fit through the window to this pore. Consequently, 1,2-dichlorobenzene would have a similar uptake to that of 1,2-dibromobenzene. When the GCMC snapshots are considered at different loadings (see Figure S10), we predict that the transverse pore is occupied at low loading levels, and the large increase in loading observed in the GCMC isotherms is a result of filling the large interior pore

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defined by the $(\gamma\text{-CD})_6$ cubes. At saturation pressures, the small triangular pore is also occupied if the adsorbate is small enough to access this pore. Upon consideration of the adsorption energies at saturation (see Table S11), it is found that 1,2-dibromobenzene has the most favorable total interaction energy (−85.5 kJ/mol), followed by 1,2-diiodobenzene (−81.6 kJ/mol) and 1,2-dichlorobenzene (−75.1 kJ/mol). Given the size constraints of CD-MOF, entropic effects are likely an important distinguishing feature for the separation of 1,2-dichloro- and 1,2-diiodobenzene.

CONCLUSIONS

The ability of CD-MOF-1 to act as a separation medium for a wide variety of compounds, including alkyl-, vinyl-, and haloaromatics, saturated and unsaturated alicyclic compounds, as well as chiral compounds, distinguishes this extended framework material from the majority of other MOFs investigated for their use as stationary-phase materials in separations. Not only is CD-MOF-1 a versatile stationary phase, but it is also readily prepared from environmentally benign and biocompatible starting materials on a large scale. In addition to the experimentally observed separations, quantum mechanical calculations and GCMC simulations were employed in order to predict the possible mechanisms through which this separation takes place. One of the main advantages of using MOFs as stationary phases over traditional amorphous materials, such as modified silicas, is that the separation behavior can be predicted by calculations, and the reasons behind such separations can be explained more comprehensively. Calculations suggest that the separation of styrene and ethylbenzene may be driven by differences in the noncovalent bonding interactions between these two compounds and isolated γ-CD rings. Examination of the separation of different mono- and disubstituted haloaromatic compounds indicates that there exists an important balance between the ability of a guest molecule to interact with the framework as well as its size and shape. Although larger halogens are predicted by quantum mechanical calculations to interact more favorably with an isolated γ-CD ring, it is likely that the size limitations imposed by the dimensions of the framework act in such a way as to prevent the achievement of the most favorable orientations for noncovalent bonding interactions. This finding is supported by GCMC simulations which show that although the total potential energy of interaction with the framework is greater than that of the smaller haloaromatic compounds, fewer molecules of the larger haloaromatics can be adsorbed within CD-MOF, suggesting that entropic factors may play a dominant role in the separation process. Quantum mechanical calculations performed on 1:1 complexes of a range of guests with γ-CD suggest that, aside from the preferential binding of styrene over ethylbenzene to an isolated γ-CD ring, the ability of CD-MOF to separate the range of compounds discussed in this full paper is a function of the emergent properties that arise from the nature of the extended framework as a whole. The versatility shown by CD-MOFs in relation to a wide range of applications indicates that the preparation of additional framework materials based on macrocyclic and/or sugar-based organic linkers could constitute a rewarding research goal and should be pursued with some zeal, in combination with theoretical considerations.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b12860.

Experimental and calculation details, separation factors (Tables S1−S8), liquid-phase HPLC (Figures S1−S6), and computational modeling and analysis (Figures S7−S13 and Tables S9−S11) (PDF)

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Notes

The authors declare the following competing financial interest(s): R.Q.S. has a financial interest in the start-up company NuMat Technologies, which is seeking to commercialize metal−organic frameworks. Y.Y.B. and J.F.S. have a financial interest in the start-up company PanaceaNano, which is seeking to commercialize CD-MOF.

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