Tunable Porosity through Cooperative Diffusion in a Multicomponent Porous Molecular Crystal

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Abstract

A combination of different molecular simulation techniques was used to begin to uncover the mechanism behind the compositional tuning of gas sorption behaviour in a multicomponent porous molecular crystal, \( \text{CC1-CC3}_n\text{CC4}_{1-n} \), where \( 0 < n < 1 \). Gas access to formally occluded voids was found to be allowed through a cooperative diffusion mechanism that requires the presence of the guest for the channel to briefly open. Molecular dynamics simulations and dynamic void analysis suggest two putative diffusion mechanisms. We propose that the gas diffusion is controlled by the cage vertices that surround the void, with the slightly smaller and more mobile cyclopentane vertices in \( \text{CC4} \) allowing more facile nitrogen diffusion than the cyclohexane vertices in \( \text{CC3} \). A combination of sorption simulations, void analysis and statistical calculations suggest the diffusion mechanism may rely upon the presence of two \( \text{CC4} \) molecules adjacent to the occluded voids.
**Introduction**

Control over function in organic crystals is important both in the pharmaceutical industry and for functional molecular materials, such as porous solids. Variation of the molecular composition in organic crystal provides the opportunity to control properties, such as gas sorption. However, multicomponent crystals with more than two independent molecular components are comparatively rare in the organic solid state because of the tendency to form separated phases. In metal-organic frameworks (MOFs), directional coordination bonding has allowed for multiple functional groups to be incorporated in a single network.\(^1\) Such multivariate (MTV) MOFs can contain up to eight different functional groups because directional bonding allows this isoreticular chemistry.\(^2\) This increased level of complexity in the materials has produced unexpected properties that are not attainable from the individual molecular building blocks alone. It is possible to control the spatial ordering of ligands in MTV-MOFs,\(^3\) suggesting the possibility of single materials containing regions with different functionalities to produce a ‘nanoscale factory’ performing multiple operations on guests. By contrast, the ability to control composition in multicomponent organic molecular crystals is rare, mainly due to a lack of strong directional bonding. Davis produced solid solutions or “organic alloys” where the composition could be varied continuously without affecting the overall structure.\(^4\) More recently, Cooper and coworkers prepared porous molecular tercrystals, whereby three different intrinsically porous organic molecules could be incorporated in the same crystal to provide both tunable molecular composition and properties.\(^5\) These molecular tercrystals lack any 3-dimensional covalent intermolecular bonding; nevertheless, the molecules in these tercrystals pack preferentially in a window-to-window fashion, thus providing a
directional packing motif that is analogous to the directional coordination bonding in reticular MOF chemistry.6

Porous molecular materials have been of growing interest in the last few years.7,8 Their porosity can originate from inefficient packing resulting in extrinsic voids,9 or from shape-persistent molecules containing an intrinsic cavity.10 The current record for the Brunauer-Emmett-Teller (BET) surface area of a porous molecular material is 3758 m² g⁻¹, as reported for a mesoporous boronic ester ‘cage’ synthesised by Mastalerz et al.10 Here, we conducted a computational investigation of our porous organic imine cage system tercrystal,5 with the aim of uncovering the mechanism behind the variation in gas sorption properties with crystal composition. These tercrystals consist of a mixture of three tetrahedral symmetry imine cages (CC1, CC3 and CC4), each with four windows that are large enough to allow diffusion of small gases. The three cages differ only by their vertex functionalisation. All three molecules are synthesised via imine condensation reactions of 1,3,5-triformylbenzene with different diamines; CC1 has unfunctionalised ethane vertices, CC3 has chiral cyclohexane vertices, and CC4 has chiral cyclopentane vertices (see Figs. 1 and S1). We were able to synthesise tercrystals of these systems by exploiting the molecules’ preference to pack (i) window-to-window and (ii) in heterochiral pairings.11 CC1 is able to switch between enantiomers of opposite chiral axial symmetry, both in solution and in the solid state,12,13 but CC3 and CC4 are not. Hence, a 1:1 ratio of enantiomers was targeted in the tercrystal; that is, an equimolar ratio of CC1 and (CC4 + CC3). Since CC1 resolves to form its S enantiomer, it was possible to mix any relative proportions of CC3-R and CC4-R to form CC1CC3,(CC4)R,R tercrystals, where 0 < n < 1, including binary cocrystals CC1/CC4-R and CC1/CC3-R where n=0 and n=1, respectively.
**Figure 1:** The three imine cages present in the tercrystal. All cages are formed from a reaction of 1,3,5-triformylbenzene with different diamines. Here, the molecular structure of each diamine is shown, together with the molecular structure of the cage and a simplified schematic. **CC1-S** is shown in green; **CC3-R** in red; and **CC4-R** in purple. The bottom right panel of the figure is a schematic showing the cubic packing in the ternary crystal, where **CC1** occupies half the sites and **CC3** and **CC4** are disordered over the other half of the sites.

For all these tercrystals, single-crystal X-ray diffraction revealed isostructural crystallisation in the cubic space group $F23$. $^5$ **CC1-S** and **CC3-R/CC4-R** occupy alternating sites in the structure, with **CC3-R** and **CC4-R** being disordered over half of the sites (Fig. 1). Most intriguing was the observation of property tuning with molecular composition: the BET surface area increased steadily with the proportion of **CC4** relative to **CC3**, from a BET surface area of 373 m$^2$ g$^{-1}$ for **CC1/CC3-R** to 670 m$^2$ g$^{-1}$ for **CC1/CC4-R**.$^5$ This corresponds to near doubling of nitrogen uptake, from 4.5 to 7.9 mmol g$^{-1}$ at P/P$_0$=0.99 and 77 K. We hypothesized that the difference
in surface area might be accounted for by differential access to certain voids as the CC4 composition is varied, but we presented no proof for this in our first study.

A schematic of the pore system in the tercrystals is shown in Fig. 2 (additional images in Figs. S2-3). There is a dominant diamondoid pore network that runs through the internal cavities of the cages (shown in yellow), with the centre of each cage forming the nodes in this network. Additionally, there are occluded voids (orange) that are extrinsic to the cage molecules themselves, but of comparable size to the cavities in the cages. It is access to these formally occluded voids that was proposed to be responsible for the porosity tuning, although no direct experimental evidence for this could be obtained.

**Figure 2:** Schematic of the pore system in the cage cocrystals and tercrystals (shown here for the binary CC1/CC4-R cocrystal), as evaluated from the static single-crystal X-ray diffraction structure. The interconnected diamondoid pore network, with the cage centres as nodes, is shown in yellow. The formally occluded sites that are extrinsic to the cage molecules are shown in orange.

Here we use computation to test the hypothesis that porosity “without pores”\(^{14}\) might explain the variation of properties in these tercrystals. Barbour coined this term
for porous crystals that are permeable to a guest, even though there are no permanent channels available for that guest’s diffusion. A classic example of this is the bowl-shaped macrocycle \( p\text{-Bu}^\prime\text{-calix}[4]\text{arene} \), which Atwood showed to be permeable to small gases and even vinyl bromide, despite being formally non-porous.\(^{15}\) What is important here is the word “permanent”: these systems are microporous, with pores typically very close in size to that of the guests. From simulations, it has been shown that dynamical motion of the host can explain guest diffusion in these molecular systems.\(^{16-19}\) There are several different potential mechanisms for diffusion of guests in formally non-porous systems. First, the guest may cause a permanent structural change of the host to a more ‘open’ phase, as is seen for the framework material MIL-53.\(^{20}\) Second, the host may not permanently rearrange, but the pore system might breathe over time, such that pore necks are temporarily large enough for a guest to ‘opportunistically’ hop through. Pore breathing effects are known to be important even in relatively rigid zeolites and MOFs when the pores are of similar size to the guests.\(^{21-23}\) Finally, ‘cooperative diffusion’ may occur, where the guest itself contributes to the opening of the pore, which again is temporary. Here, a temporary alteration of the host occurs that would not arise in the absence of the guest. This is analogous to the ‘peristaltic’ motion used when food is swallowed and moved through the oesophagus. This mechanism is postulated for porous molecular materials and has been observed on many occasions for ‘flexible’ MOFs, often being a positive effect that can promote selectivity.\(^{24,25}\) No permanent phase change was observed for our cage tercystals upon gas loading, and hence it is likely that either opportunistic or cooperative diffusion mechanisms are at play.

It is challenging to consider the influence of dynamical motion of the host porous material over time, particularly when attempting to observe what may be rare
diffusion events that occur on a timescale longer than that which is feasible within a molecular simulation. Also, these multicomponent cage crystals are complex, and the pore structures are not trivial to visualize in 3-dimensions; this is additionally challenging here given the disorder of the CC3 and CC4 molecules in the tercrystals. To assist with this, we have recently developed sophisticated analysis approaches,\textsuperscript{17} employing Zeo++ software,\textsuperscript{26} to allow for quantification and visualization of the evolution of pore topologies. Here we apply these techniques, in combination with molecular dynamics (MD), gas sorption simulations, and a statistical sorption model, in order to uncover the mechanism behind porosity tuning in these cage tercrystals. We also carried out additional experimental sorption measurements on hydrogen gas in the cocrystals.

**Methods**

Gas sorption measurements were carried out for H\textsubscript{2} adsorption and desorption at 77 K in the cocrystals, see Supporting Information for further details. Where a cage in the tercrystal can be either CC3 or CC4, we will refer to it throughout as CCX. We first analysed the voids for the previously reported single-crystal X-ray structures in the Cambridge Crystallographic Database for the cocrystals CC1/CC3-R (CCDC reference number 793897)\textsuperscript{27} and CC1/CC4-R (CCDC 876253)\textsuperscript{5}. Any disordered nitrogen gas was deleted \textit{in silico} and the slight disorder of the CC4 cyclopentane vertices was removed through arbitrarily selecting the vertex orientation (the vertex was observed to visit both sites during MD simulations). For void analysis, Zeo++\textsuperscript{26,28} was used, which in addition to calculating void space also includes a Voronoi decomposition in order to determine the interconnectivity of this void space. Surface area accessible to N\textsubscript{2} was calculated with a probe radius of 1.82 Å, equivalent to the
kinetic radius of $N_2$. The atomic radii for the host were taken from the Cambridge Crystallographic Database Centre (CCDC) guidelines. Grand Canonical Monte Carlo (GCMC) simulations were performed on the two cocrystal structures using the RASPA code developed by D. Dubbeldam, S. Calero, D. E. Ellis, R. Q. Snurr. The Lennard-Jones parameters for the cages were taken from the all-atom OPLS forcefield, for $N_2$ from the TraPPE forcefield and for $H_2$ from Levesque et al. (see Supporting Information for further details).

As each of the occluded site in the cocrystals and tercrystals is surrounded by four CCX, we postulated that alternative mechanisms could underlie any potential $N_2$ diffusion mechanism, whereby access to the occluded sites is possible when (i) 1; (ii) 2; (iii) 3 or (iv) 4 of these cages are CC4 (with correspondingly 3, 2, 1 or 0 CC3 molecules). We assume in all scenarios that when there are no CC4 molecules, none of the occluded sites are accessible to $N_2$. As the four CCX have a tetrahedral arrangement around the occluded void (see Fig. 3a and Movie S1), then all arrangements of CCX are symmetry equivalent and thus there is no difference in where the CC4 is sited in any scenario. We take the CC1/CC3-R experimentally measured BET surface area of 373 m$^2$ g$^{-1}$ as the minimum surface area, when the proportion of CC4 is 0%. As we had found from the Zeo++ calculations that the occluded voids correspond to ~40% of the total surface area, we therefore calculate that the total occluded volume corresponds to 248 m$^2$ g$^{-1}$ (assuming 373 m$^2$ g$^{-1}$ is 60% of total possible surface area), this corresponds to 62 m$^2$ g$^{-1}$ ascribable to each occluded site. Next, we calculated the probability that each of the 4 scenarios occurs at different proportions of CC4, assuming that the sites of the CC4 with respect to each other are randomly distributed in the tercrystal (i.e. not clustered). Finally, we calculated the total surface area at each proportion for each scenario through
multiplying the probability of access by the occluded volume surface area and adding this to the main network surface area. These calculations do not factor in any cell compression as the proportion of the CC4 cage is increased, but the calculations are carried out in Å² before converting to m² g⁻¹, with the mass of the system adjusted according to the proportion of CC4.

**Figure 3:** (a) Schematic of the environment surrounding the occluded sites; each site is surrounded by four CCX molecules (purple) arranged in a tetrahedral arrangement and six CC1 molecules (green) arranged in an octahedral arrangement around the occluded site (orange). (b) The first possible route out of the occluded site passes three CCX vertices to an adjacent occluded site. (c) The second possible route is to diffuse into the main diamondoid network by passing between two cage windows.

MD simulations were first carried out on the empty host cocrystals, combined with the use of Zeo++ to analyse how the pores evolve over time; this allowed us to explore dynamic pore connectivity, as we have done previously for CC3.¹⁷ MD simulations were run in the NPT ensemble with DL_POLY2.20³⁴ and the all-atom OPLS forcefield,³¹ which we have previously demonstrated to be successful in reproducing the structure and energetics of porous organic imine cages.³⁵ Production runs of 1 ns were sampled every 1 ps (see Supporting Information for further details).
We have previously developed an approach to visualize evolving pore topology over time, allowing pore opening and closing events to be observed and, further, a method by which the complete dynamic host system over time can be visualized as a single figure we call a ‘void histogram’, to view many hundreds or thousands of pore breathing events simultaneously. This dynamical pore analysis was carried out for the N$_2$ probe radius of 1.82 Å and for a probe radius of 1 Å, the latter to observe the smallest intrinsic channels, albeit those too small for any gas to diffuse through.

To observe potential diffusion of gases, MD simulations were performed with a single H$_2$ or N$_2$ molecule, starting in an occluded site, in the two cocrystal supercells. The gases were modelled with potentials previously reported in the literature for H$_2$ and N$_2$, with all other details as reported above for the empty host simulations. Simulations were also performed with the cocrystals fully loaded with H$_2$ molecules, with the configuration taken from the 1 bar GCMC simulation where all sites were accessible. For CC1/CC3-R, this corresponded to 9.0 H$_2$ molecules per cage molecule and for CC1/CC4-R to 8.4 H$_2$ molecules per cage molecule.

**Results and Discussion**

**Pore network evaluated from the crystal structure**

We first investigated the void structure from an analysis of the cocrystal CC1/CC3-R and CC1/CC4-R single-crystal X-ray structures, as detailed in Table 1. The largest cavity in the structures is the occluded void, which is roughly spherical, and of diameter 7.06 Å for CC1/CC3-R and 6.73 Å for CC1/CC4-R. The size of the cage voids is, as expected, similar in both cocrystals, although smaller than the occluded sites with a diameter of ~5.6 Å. The pore-limiting diameter, which is the narrowest point in the interconnected channel, is 3.77 Å for CC1/CC3-R and 3.61 Å for CC1/CC4-R. The pore-limiting diameter corresponds to the cage window and this
shows how the CC1/CC4-R system has a slightly narrower window, which suggests from a static viewpoint that no N₂ molecules should be able to diffuse through the CC1/CC4-R system (the kinetic diameter of N₂ is 3.64 Å). The surface area for N₂ with this probe is calculated in total as 793 m² g⁻¹ for CC1/CC3-R and 595 m² g⁻¹ for CC1/CC4-R. Zeo++ further allows us to determine the proportion of this surface that is interconnected across the unit cell for this probe; this corresponds to ~60% of the surface area in both systems and is entirely resulting from the main diamondoid network running through the cages. The remaining ~40% of the surface area is attributed to the formally occluded sites. Interestingly, this difference in the occluded and main network surface area is very similar to the differences in the cocrystal systems found experimentally, where the CC1/CC3-R system has approximately 44% less BET surface area than the CC1/CC4-R system. This supports the hypothesis that the introduction of CC4 into the ternary system allows for increasing access to the occluded site and therefore increasing surface area with the proportion of CC4. What is striking is that the less dense CC1/CC3-R system has a larger calculated total surface area than CC1/CC4-R by 198 m² g⁻¹; as such, it is clear that an analysis of the static crystal structures alone can not explain the experimentally observed higher N₂ uptake in CC1/CC4-R.
Table 1: The key values from the void analysis of the cocrystal systems. The surface areas (SA) are calculated with a probe radius of 1.82 Å.

|                                      | CC1/CC3-R | CC1/CC4-R |
|--------------------------------------|-----------|-----------|
| Largest cavity diameter (Å)          | 7.06      | 6.73      |
| Pore limiting diameter (Å)           | 3.77      | 3.61      |
| Cage void diameter (Å)               | 5.63      | 5.58      |
| Interconnected SA (m² g⁻¹)           | 458       | 366       |
| Formally disconnected SA (m² g⁻¹)    | 335       | 229       |
| Total SA (m² g⁻¹)                    | 793       | 595       |
| Proportion of interconnected SA (%)  | 58        | 62        |
| BET SA from experiment (m² g⁻¹)      | 373       | 670       |

Sorption measurements and simulations

Whilst we had previously observed N₂ sorption to vary according to the composition of the tercrystal,⁵ here we found that this change in gas uptake across compositions was not observed for H₂; at P/P₀=0.99 and 77 K, uptakes of ~7.4-7.6 mmol g⁻¹ where observed that were essentially independent of the tercrystal composition (Fig. S4). To investigate whether access to the occluded sites could explain the differences in the gas sorption behaviour, GCMC simulations were performed on the two cocrystals for N₂ and H₂. A systematic small overestimation of uptake has been previously reported for gas sorption in extrinsically porous organic crystals⁶ and in porous organic cages, both for CO₂⁷ and noble gas sorption,⁸ and this is also observed for H₂ in these cocrystals. In the report of noble gas sorption in CC3, the ε values of the Lennard-Jones interactions that correspond to the strength of the host-guest interactions were
reduced by a factor of 0.69 in order to prevent the overestimation of gas uptake.\textsuperscript{39} We have chosen not to do that here as we have varying mixtures of the three cage molecules in the crystals, so the correction factor might not be uniformly applied. We do, however, expect a small overestimation of guest uptake in our simulations.

The calculated isotherms for H\textsubscript{2} are shown in Fig. S4. Access to all sites, including the occluded sites, gives the best match to experimental isotherms, with a small overestimation of uptake in the simulations. Access to all sites in all crystals would also fit with the very similar gas uptakes observed for H\textsubscript{2} across all the cocrystals and tercrystals. The calculated isotherms for N\textsubscript{2} are particularly interesting, and are shown in Fig. 4. Here we can see that for both cocrystal systems, the simulated saturation uptake at 1 bar, when all sites are accessible is very similar: the uptake is 9.2 mmol g\textsuperscript{-1}. For CC1/CC4-\textit{R}, this is in reasonable agreement with the experimental saturation uptake of 8.1 mmol g\textsuperscript{-1}, allowing for a small overestimate in the simulation (by \textasciitilde14\%). For comparison, simulations where the occluded sites are blocked would underestimate the experimental uptake by 38\%. The best match to experiment, therefore, is made with the assumption that all the occluded sites are accessible to N\textsubscript{2} in CC1/CC4-\textit{R}.

For CC1/CC3-\textit{R}, by contrast, the simulated sorption into all of the sites would correspond to an overestimation of N\textsubscript{2} sorption with respect to experiment of 70\%; that is, much greater than could reasonably be explained by any forcefield overestimation. However, when the occluded sites are blocked, the simulated uptake is in very good agreement with the experiment, with an overestimation of just 8\%. From the GCMC simulations, we can therefore surmise that the occluded sites are accessible for H\textsubscript{2} in all systems, but for N\textsubscript{2} they are only accessible in CC1/CC4-\textit{R},
and not in CC1/CC3-R. The differences can be explained by the increasing kinetic radii$^{29}$ across these gases; $1.45 \ \text{Å} \ (\text{H}_2) < 1.82 \ \text{Å} \ (\text{N}_2)$.

**Figure 4:** Predicted nitrogen uptake at 77 K for CC1/CC3-R (red) and CC1/CC4-R (purple) compared to previous experimental results$^5$ in black. The GCMC simulations were carried out with all sites accessible (solid lines) and with the formally occluded sites blocked (dashed lines).

**Statistical modelling of surface area**

The GCMC results suggested that increasing accessibility to the occluded sites with increasing proportion of CC4 molecules might explain the experimentally observed increase in BET surface area and N$_2$ uptake. We next wanted to investigate the underlying mechanism behind this. In all cocrystals and tercrystals, four CCX molecules surround the occluded sites in a tetrahedral arrangement (Fig. 3a), and hence between 0 and 4 of these CCX molecules could potentially be CC4 (for the
CC1/CC4-R cocystal, of course, all 4 CCX molecules would be CC4). Assuming that at least one CC4 molecule is required to be present for N₂ diffusion into the occluded void (that is, the CC1/CC3-R excludes N₂ from these voids), then there are potential diffusion mechanisms that require between 1 and 4 CC4 molecules to surround the void such that N₂ diffusion is allowed. To explore this, we therefore applied a statistical model, first to determine the probability of each diffusion scenarios as a function of CC4 composition, and then to account for the additional surface area from the accessible occluded voids for each diffusion scenario.

The statistically modelled surface areas with respect to CC4 proportion for each of these scenarios is shown in Fig. 5, and is compared to the experimentally reported BET surface areas for the various tercrystal compositions. It is clear that the best match to experiment is given by the scenario in which a minimum of 2 of the CCX molecules surrounding the occluded site needs to be CC4 to allow N₂ diffusion. Given the tetrahedral arrangement of the CCX molecules, the exact positioning of the CC4 molecules around the site is not important, because they are all symmetry equivalent. In all of these models, there is a failure to reproduce the slight decrease in experimental BET surface areas at the highest CC4 proportion of 50%. It was postulated previously that this is a result of an increase in structural rigidity when forming the pure CC1/CC4-R binary cocystal, which has no disorder compared to the three component tercrystals.⁵ This is something that would not be accounted for in our simple statistical model here. We also note that the degree of crystallinity can significantly alter the measured surface area, even with materials that are apparently crystalline; for example ‘crystalline’ CC3 surface area can range from 409\(^1\) to 624 m\(^2\) g\(^{-1}\),⁴⁰ although careful crystallisation results in consistent surface areas with a very small standard deviation across samples of 409 ± 9 m\(^2\) g\(^{-1}\).¹¹
Figure 5: An analysis of the surface area predicted for tercrystals with varying proportions of CC4. Four different scenarios for occluded site accessed are assumed, requiring a minimum of one, two, three, or all four of the four CCX sites to be CC4 in order to allow diffusion. For this plot, 0% corresponds to the binary cocrystal, CC1/CC3-R, and 50% to the binary cocrystal CC1/CC4-R. These statistical models are compared to the previously reported experimental measurements (black diamonds).  

**Dynamic porosity through dynamic pore connectivity**

The statistical models suggest that, on average, two of four CCX molecules must be CC4 in order for N2 diffusion to occur into the occluded voids. We next sought to uncover the underlying atomistic mechanism behind this. If the occluded site is considered again (Fig. 3a), then although no channels connect it to the main network, on closer examination we could suggest two possible, albeit superficially unlikely, routes. The first of these, shown in Fig. 3b, is for diffusion directly between occluded sites, without connecting to the main diamondoid network. This route would require a guest travelling a distance of ~10.0 Å between the two voids, which is similar to the
distance between the centres of window-to-window packed cages of ~10.4 Å (see Table S1). Traversing this distance seems to be a significant challenge for the guest, although we note that a secondary, interpenetrated, diamondoid network between occluded sites has previously been found with MD simulations for the porous organic cage CC13.6

The second route, shown in Fig. 3c, would involve the guest moving between the interlocking arms of a CC1/CCX pair and into the window site between them, thus joining the main interconnected network. This route requires the guest to travel a much shorter distance of ~4.2 Å. This is not a mechanism that we have previously observed, and it would be relatively unexpected given the strong racemic binding between the cage pairs.11 For this route, which involves directly only one CC4 molecule, it is not obvious how this could relate with the previous statistical models that suggest that the mechanism is dependent on two neighbouring CC4 molecules.

We next used our recently developed approach17 to examine the dynamical evolution of the pores in the cocrystal systems over time during MD simulations. First, we determined how the occluded site itself evolves over a 1 ns simulation, creating void histograms, as shown in Fig. 6, which show all the voids accessible for between 0.05–50% of the simulation time for a N2 probe. The image shown is for CC1/CC4-R, but the same behaviour was also observed for CC1/CC3-R. For 50% of the simulation (Fig. 6a), we observed that the void was very similar in size to that of the static crystal structure, and there are no channels opening up towards either of our identified potential ‘escape routes’ (indicated by arrows in Fig. 6a). However, as we look at voids open for smaller fractions of the simulation time in Figs. 6b and c, we see that the void becomes larger, with voids progressing toward both of the escape routes, but with no complete channel opening up in either direction. For the escape
route to the neighbouring occluded site, we see the void reaches right up to three CC4 vertices, which block access to the next site on their far side. It would appear that these three vertices are acting as ‘gate-keepers’ with respect to that diffusion route.

Figure 6: Dynamical pore analysis for CC1/CC4-R; the void histograms showing voids accessible (red) to a N$_2$ probe of radius 1.82 Å over a 1 ns MD simulation for (a) 50%, (b) 5%, and (c) 0.05% of the sampled configurations. In (a) the two potential ‘escape routes’ are shown with yellow arrows; (top) to the next occluded site past the three CCX ‘gate keeper’ vertices or (bottom) between the two cage window sites into the diamondoid network. The same behaviour was observed for CC1/CC3-R.

While no channels were observed to open up from the occluded site with a N$_2$ probe radius of 1.82 Å, we were, however, able to observe the occluded site becoming connected to adjacent voids if we decreased the probe radius to 1 Å, which is smaller than even H$_2$ gas. We were able to watch these channels over time, coloured in Zeo++ according to their connectivity, with the occluded sites initially shown in red as they are isolated and the main network shown in green as it is interconnected (see Fig. 7 and S5). Since the 3-dimensional pore structure is difficult to represent for these structures, we focus here on the environment around just one occluded site in
**CC1/CC3-R** (the same behaviour is seen for **CC1/CC4-R**). The evolution of the pores over time is seen in Movie S2, with key events shown in Fig. 7b-d. In Fig. 7c, the occluded site has turned green (interconnected) because a channel has opened up to the main network, through a gap between the cage windows, as in the schematic mechanism shown in Fig. 3c. In Fig. 7d, the occluded site has formed a small channel to an adjacent occluded site, through ‘gate keeper’ **CC4** vertices, as in the mechanism shown in Fig. 3b. We were therefore able to observe the potential for both mechanisms to occur in simulations, albeit not for probe sizes that are comparable to even small gases. As such, these guest-free simulations do not support ‘opportunistic’ diffusion of gases into the occluded sites. We did, however, observe that the temporary channel for occluded-site-to-occluded-site diffusion is larger than for occluded-site-to-main-channel diffusion (compare Fig. 7c and 7d). In contrast to these findings of pores smaller than H$_2$ gas, our previous work on **CC3**$^{17}$ indicated pores that were ‘open’ in dynamical simulations for all gases that were found to be adsorbed in experiments; as such, diffusion could be described as ‘opportunistic’, and diffusion was deemed possible without invoking cooperativity with the guest. By contrast, these new simulations suggest that diffusion in these cocrystal and tercrystals might be slow, and that it must occur by a cooperative mechanism.
Figure 7: Dynamical changes in the pore system surrounding a central occluded site in $\text{CC1/CCX-R}$. The tercrystal shown is $\text{CC1/CC3-R}$, but the same changes were observed, with no notable differences for $\text{CC1/CC4-R}$. The voids accessible to a probe of 1 Å radius are shown in green and isolated voids shown in red. (a) A $2 \times 2 \times 2$ supercell viewed down the $b$-axis (an alternative view is shown in Fig. S5). For (b)-(d) voids within a sphere of radius 12 Å from the centre of a single occluded site are shown only; (b) the central void, as it exists for the majority of the simulation time. The void is occluded (red), while the channel through the surrounding cages is interconnected (green). (c) For a few sampled configurations, the occluded site has become interconnected to the main network through the route shown in Fig. 3(c), at least with respect to this 1 Å probe radius, with a small channel opening (shown here at the bottom of the image, highlighted by an orange circle). (d) For a few sampled configurations, the occluded site has become connected to an adjacent occluded site through the route shown in Fig. 3(b); the connecting channel can be seen at the top.
right of the image (highlighted by an orange circle). This is not associated with a
colour change (the void remains red), because the void is not simultaneously
connected to the main pore network.

Gas diffusion mechanism

We next attempted to observe specific gas diffusion events with the guest molecules
present in the crystal, in order to uncover precise information about any diffusion
mechanisms and, in particular, to see whether the presence of the guest molecules
promotes pore opening compared to the previous empty-host simulations. When we
performed simulations in both of the two binary cocrystals with a single N₂ molecule
present, we did not observe any N₂ diffusion out of the occluded site over 10 ns
simulations. We also tried starting the N₂ molecule in the main channel, and while we
observed the N₂ to diffuse through the entire diamondoid network during the
simulation, we never observed the N₂ molecule to diffuse into an occluded site within
a 10 ns simulation. We believe this suggests that diffusion into or out of the occluded
sites is a rare event, happening only on a multi-nanosecond timescale, which would
agree with our MD results on the empty host crystals.

We next ran MD simulations with a single H₂ molecule present. In this case,
we observed gas diffusion via both of our postulated mechanisms in both of the
binary cocrystals, CC1/CC3-R and CC1/CC4-R. In Fig. 8a, an overlay of the host
and guest structures during a ‘hop’ between the main channel and the occluded site is
shown for CC1/CC3-R. Fig. 8b shows the H₂ molecule at the intermediate site and
Movie S3 shows the whole hopping event. This event occurs over a period of ~5 ps
and does not involve very significant displacement of the hosts beyond their natural
dynamical motion. In Fig. 8c, an overlay of the host and guest structures during a
‘hop’ between occluded sites in CC1/CC4-R is shown, with Fig. 8d showing the H₂ molecule at the intermediate site and Movie S4 showing the whole event. The whole event occurs over a period of ~10 ps, and it is clear that the H₂ molecule moves between two of the gate-keeping CC4 vertices, with both being displaced during the event. As highlighted in Fig. 8d, one CC4 vertex in particular is displaced significantly, much more so than in the normal dynamical motion of the host. Movie S5 also shows this diffusion event, but with only the vertices shown, which highlights the extent of their displacement. While we did not observe these mechanisms in 10 ns for N₂, we expect the same diffusion routes as for H₂, since both diatomic molecules have the same shape, with N₂ being larger.
**Figure 8:** Diffusion events observed during MD simulations of H$_2$. (a) An overlay of sampled configurations during diffusion between the occluded site and the diamondoid channel through moving between two cages in CC1/CC3-R. (b) The configuration during the middle of the diffusion when the H$_2$ is between the two sites. (c) An overlay of sampled configurations during diffusion between two occluded sites in CC1/CC4-R. (d) The configuration during the middle of the diffusion when the H$_2$ is between the two sites and at the gateway guarded by three CC4 vertices. The H$_2$ is observed to move between two vertices, with one ‘gate keeper’ vertex in particular moving away from the diffusion path (highlighted with an orange circle). H$_2$ molecules are shown in blue.

We next wanted to confirm that both mechanisms occurred in both cocrystal systems, and how frequently they were occurring, so we developed software to quantify the different hopping events (see Supplementary Information for more details) and performed this on 10 ns MD simulations at 298 K for the cocrystals fully loaded with H$_2$ from the GCMC simulations, such that we could observe more diffusion events to generate statistics. Simulations were not carried out at the actual temperature of the sorption experiments, 77 K, because the diffusion events are rare events that happen only a few times over the simulation time, even at the artificially high simulation temperature of 298 K. The results are shown in Table 2 and Fig. S6. The key types of diffusion events are shown in Fig. S7. Even for H$_2$, the diffusion events are very rare, thus even with the quantification from the analysis, we can not draw confident conclusions about the relative frequencies from the 10 ns simulation. The most frequent diffusion was between the main network and occluded site, occurring on average between every 28 ps (CC1/CC3-R) and every 333 ps.
(CC1/CC4-R) per cage molecule in the system. This difference can be rationalized by the fact that CC1/CC3-R, with its slightly larger vertices, is packed less densely than CC1/CC4-R, with unit cell dimensions of ~24.5 Å compared to ~23.8 Å. The window-to-window packing is therefore not as close for CC1/CC3-R, with a cage-centre-to-cage-centre distance 0.3 Å greater than for CC1/CC4-R (Table S1). The fact that the CC1/CC3-R cage pair is packed together less tightly would naturally result in diffusion between them being more facile than for CC1/CC4-R. The diffusion between the main channel and the occluded site occurs via an observably smaller channel than the occluded site-occluded site diffusion (Fig. 7). Also, there is less opportunity for the core part of the molecules to be displaced compared to the vertices of the cages. We therefore suggest that the diffusion in and out of the main channel may only be possible for small molecules, such as H₂, during the room temperature simulations, and that this mechanism should not play a significant role, if any, for larger gases such as N₂ at 77 K. Rather, for N₂, the dominant diffusion mechanism is more likely to be between occluded sites, moderated by the cage-vertex ‘gate keepers’. The observed strong hysteresis for H₂ sorption at 77 K in CC1/CC3-R, which is not seen for CC1/CC4-R (Fig. S2), would suggest slower H₂ diffusion in CC1/CC3-R and hence that the occluded site-occluded site mechanism may be dominant even for H₂ at 77 K.
Table 2: The number of different diffusion events in H$_2$ loaded cocrystal simulations over 10 ns MD simulations. The numbers quoted are for number of events per cage molecule in the host over the time period.

|                          | CC1/CC3-$R$ | CC1/CC4-$R$ |
|--------------------------|-------------|-------------|
| Diffusion to and from main channel | 36          | 3           |
| Diffusion between occluded sites | 21          | 16          |

**Discussion**

Through a combination of the empty host and gas-loaded simulations, we now have evidence for a cooperative diffusion mechanism, where the presence of the guest contributes to pore opening. The guest molecule assists in displacing two ‘gate keeper’ CC4-vertices, hence opening up the channel between occluded sites. While cooperative diffusion has often been postulated for porous molecular materials, this is a rare example of evidence for this occurring, and a counter-example of the close structural analogue (CC1/CC3-$R$) where this does not occur because the equivalent cyclohexane ‘gate keepers’ are larger. Diffusion of N$_2$ in CC1/CC4-$R$ by hopping directly between occluded sites is the most likely diffusion mechanism, although unfortunately we were unable to directly observe this in the molecular dynamics simulations. This diffusion mechanism alone would be sufficient to allow for sorption into the occluded sites, because they can interconnect to form a secondary pore network, as previously postulated in the CC13 porous imine cage system.

Furthermore, the diffusion path between occluded sites would also explain the finding from the statistical modelling that only two of the four CCX molecules surrounding an occluded site need to be CC4 molecules. This is a result of the guest molecules...
diffusing past only two of the three ‘gate-keeping’ vertices. Thus if two vertices are CC4 cyclopentanes, this is sufficient for the cooperative gas diffusion to occur.

If we assume that the critical mechanism for diffusion of N2 into occluded sites in these systems is between the occluded sites, there is one remaining question – why would occluded site diffusion be more facile for CC1/CC4-R than CC1/CC3-R? Obviously the cyclopentane (CC4) vertices are less bulky than the cyclohexane (CC3) vertices, as they have one less CH₂ group. Furthermore, the cyclopentane vertex is more mobile than the cyclohexane vertex, as observed in the single-crystal X-ray structure, where there is structural disorder of the cyclopentane-tip carbon, with two positions at 0.75 Å distance from each other being partially occupied. This same motion is seen in the empty host MD simulations at 298 K, with the root mean square displacement (RMSD) of the cyclopentane carbons of 1.89 ± 0.12 Å being significantly greater than that of the cyclohexane carbons in CC1/CC3-R, 0.53 ± 0.13 Å. This difference is also apparent in the vertex overlay in Fig. S8. As a result of this reduced bulk and greater mobility for the CC4 vertices, we can postulate that the N₂ molecule would be able to displace these gates and diffuse through the resulting temporary channel as long as two CC4 molecules are present.

Conclusions

We have determined that a cooperative diffusion mechanism is responsible for diffusion of small guest molecules into and out of the formally occluded sites in the CC1 CC3ₙ CC4ₙ₋ₙ (0 < n < 1) tercrystals. The simulations suggest that access to formally occluded sites is possible so long as at least two of the four molecules surrounding an occluded site are CC4 rather than CC3. Whilst we were unable to directly observe N₂ diffusion in the molecular simulations, we postulate that the
presence of the smaller, more mobile cyclopentane vertices in CC4 would aid the N2 diffusion and hence explain the experimental observation of increased nitrogen uptake with higher CC4 ratio tercrystals. These tercrystals are particularly complex systems to investigate and this, combined with the role of dynamical motion of the host, means that a combination of simulations and new computational analysis tools was required to observe the cooperative diffusion behaviour. We believe the ability to explain, and consequently predict, the diffusion behaviour in porous molecular systems is important if we are able to achieve our long-term goal of de novo design in these systems. We previously demonstrated that we can predict the cage reaction outcomes from the reaction precursors,35 and that it is possible to predict the 3-dimensional solid state structure through crystal structure predictions.27 Combined with the porosity analysis tools used here, these means we can in principle start from a 2-dimensional chemical sketch of the cage precursors and predict complex solid state dynamic properties for this class of system.

There are many opportunities for tuning of sorption properties in multicomponent porous molecular systems, particularly in accessing unique chemical selectivities and sorption capacities that may not be achievable from single component systems – for example, to carry out specific molecular separations.25 For porous cages, recent experimental work has shown that the cage packing can be engineered towards window-to-window packing through a directing solvent, even for cages where this is not necessarily the native packing mode.6 This opens the door to extend these multicomponent systems to include many other cage modules, and to access more diverse properties and even greater tunability. Porous molecular materials have also shown promise in catalysis41 and in sensing,42,43 and control of multicomponent systems might therefore allow tuning of multiple functionalities.
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Supporting information description

The supporting information contains additional methods, tables, figures and movies.

References

(1) Deng, H.; Doonan, C. J.; Furukawa, H.; Ferreira, R. B.; Towne, J.; Knobler, C. B.; Wang, B.; Yaghi, O. M. Multiple Functional Groups of Varying Ratios in Metal-Organic Frameworks. Science 2010, 327, 846–850.

(2) Yaghi, O. M.; O’Keefe, M.; Ockwig, N. W.; Chae, H. K.; Eddaoudi, M.; Kim, J. Reticular Synthesis and the Design of New Materials. Nature 2003, 423, 705–714.

(3) Kong, X.; Deng, H.; Yan, F.; Kim, J.; Swisher, J. A.; Smit, B.; Yaghi, O. M.; Reimer, J. A. Mapping of Functional Groups in Metal-Organic Frameworks. Science 2013, 341, 882–885.

(4) Natarajan, R.; Magro, G.; Bridgland, L. N.; Sirikulkajorn, A.; Narayanan, S.; Ryan, L. E.; et al. Nanoporous Organic Alloys. Angew. Chem. Int. Ed. 2011,
(5) Hasell, T.; Chong, S. Y.; Schmidtmann, M.; Adams, D. J.; Cooper, A. I. Porous organic alloys. *Angew. Chem. Int. Ed.* 2012, 51, 7154–7157.

(6) Hasell, T.; Culshaw, J. L.; Chong, S. Y.; Schmidtmann, M.; Little, M. A.; Jelfs, K. E.; Pyzer-Knapp, E. O.; Shepherd, H.; Adams, D. J.; Day, G. M.; et al. Controlling the crystallization of porous organic cages: molecular analogs of isoreticular frameworks using shape-specific directing solvents. *J. Am. Chem. Soc.* 2014, 136, 1438–1448.

(7) Slater, A. G.; Cooper, A. I. Function-led design of new porous materials. *Science* 2015, 348, DOI: 10.1126/science.aaa8075.

(8) Zhang, G.; Mastalerz, M. Organic cage compounds – from shape-persistency to function. *Chem. Soc. Rev.* 2014, 43, 1934–1947.

(9) Mastalerz, M.; Oppel, I. M. Rational construction of an extrinsic porous molecular crystal with an extraordinary high specific surface area. *Angew. Chem. Int. Ed.* 2012, 51, 5252–5255.

(10) Zhang, G.; Presly, O.; White, F.; Oppel, I. M.; Mastalerz, M. A permanent mesoporous organic cage with an exceptionally high surface area. *Angew. Chem. Int. Ed.* 2014, 53, 1516–1520.

(11) Hasell, T.; Chong, S. Y.; Jelfs, K. E.; Adams, D. J.; Cooper, A. I. Porous organic cage nanocrystals by solution mixing. *J. Am. Chem. Soc.* 2012, 134, 588–598.

(12) Jones, J. T. A.; Holden, D.; Mitra, T.; Hasell, T.; Adams, D. J.; Jelfs, K. E.; Trewin, A.; Willock, D. J.; Day, G. M.; Baesa, J.; et al. On-off porosity switching in a molecular organic solid. *Angew. Chem. Int. Ed.* 2010, 123, 775–779.
(13) Jelfs, K. E.; Schiffmann, F.; Jones, J. T. A.; Slater, B.; Cora, F.; Cooper, A. I. Conformer interconversion in a switchable porous organic cage. Phys. Chem. Chem. Phys. 2011, 13, 20081–20085.

(14) Barbour, L. Crystal porosity and the burden of proof. Chem. Commun. 2006, 1163–1168.

(15) Atwood, J. L.; Barbour, L.; Jerga, A.; Schottel, B. L. Guest transport in a nonporous organic solid via dynamic van der Waals cooperativity. Science 2002, 298, 1000–1002.

(16) Jelfs, K. E.; Cooper, A. I. Molecular simulations to understand and to design porous organic molecules. Curr. Opin. Solid State Mater. Sci. 2013, 17, 19–30.

(17) Holden, D.; Jelfs, K. E.; Trewin, A.; Willock, D. J. Gas diffusion in a porous organic cage: analysis of dynamic pore connectivity using molecular dynamics simulations. J. Phys. Chem. C 2014, 118, 12734.

(18) Jiang, S.; Jelfs, K. E.; Holden, D.; Hasell, T.; Chong, S. Y.; Haranczyk, M.; Trewin, A.; Cooper, A. I. Molecular dynamics simulations of gas selectivity in amorphous porous molecular solids. J. Am. Chem. Soc. 2013, 135, 17818–17830.

(19) Evans, J. D.; Huang, D. M.; Hill, M. R.; Sumby, C. J.; Thornton, A. W.; Doonan, C. J. Feasibility of mixed matrix membrane gas separations employing porous organic cages. J. Phys. Chem. C 2013, 118, 1523-1529.

(20) C. Serre, F. Millange, C. Thouvenot, M. Noguès, G. Marsolier, A. D. Louër, G.Férey, Very large breathing effect in the first nanoporous chromium(III)-based solids: MIL-53 or CrIII(OH)·{O2C–C6H4–CO2}·{HO2C–C6H4–CO2H}x·H2Oy. J. Am.
Chem. Soc. 2002, 124, 13519–13526.

(21) Haldoupis, E.; Watanabe, T.; Nair, S.; Sholl, D. S. Quantifying Large Effects of Framework Flexibility on Diffusion in MOFs: CH4 and CO2 in ZIF-8. 2012, 13, 3449–3452.

(22) Awati, R. V.; Ravikovitch, P. I.; Sholl, D. S. Efficient and Accurate Methods for Characterizing Effects of Framework Flexibility on Molecular Diffusion in Zeolites: CH4 Diffusion in Eight Member Ring Zeolites. 2013, 117, 13462–13473.

(23) Vlugt, T. J. H.; Schenk, M. Influence of Framework Flexibility on the Adsorption Properties of Hydrocarbons in the Zeolite Silicalite. J. Phys. Chem. B 2002, 106, 12757–12763.

(24) Warren, J. E.; Perkins, C. G.; Jelfs, K. E.; Boldrin, P.; Chater, P. A.; Miller, G. J.; Manning, T. D.; Briggs, M. E.; Stylianou, K. C.; Claridge, J. B.; et al. Shape selectivity by guest-driven restructuring of a porous material. Angew. Chem. Int. Ed. 2014, 53, 4592–4596.

(25) H. Sato, W. Kosaka, R. Matsuda, A. Hori, Y. Hijikata, R. V. Belosludov, S. Sakaki, M. Takata, and S. Kitagawa, Self-accelerating CO sorption in a soft nanoporous crystal, Science 2014, 343, 167–170.

(26) Willems, T. F.; Rycroft, C. H.; Kazi, M.; Meza, J. C.; Haranczyk, M. Algorithms and tools for high-throughput geometry-based analysis of crystalline porous materials. Micropor. Mesopor. Mater. 2012, 149, 134–141.

(27) Jones, J. T. A.; Hasell, T.; Wu, X.; Bacsa, J.; Jelfs, K. E.; Schmidtmann, M.; Chong, S. Y.; Adams, D. J.; Trewin, A.; Schiffman, F.; et al. Modular and predictable assembly of porous organic molecular crystals. Nature 2011, 474, 367–371.
(28) Pinheiro, M.; Martin, R. L.; Rycroft, C. H.; Haranczyk, M. High accuracy geometric analysis of crystalline porous materials. *Cryst. Eng. Comm.* **2013**, *15*, 7531–7538.

(29) Robeson, L. M. Correlation of separation factor versus permeability for polymeric membranes, *J. Membr. Sci.* **1991**, *62*, 165–185.

(30) http://www.ccdc.cam.ac.uk/products/csd/radii.

(31) Jorgensen, W. L.; Maxwell, D.; Tirado-Rives, J., Development and testing of the OPLS all-atom force field on conformational energetics and properties of organic liquids. *J. Am. Chem. Soc.* **1996**, *118*, 11225–11236.

(32) Potoff, J. J.; Siepmann, J. I., Vapor–liquid equilibria of mixtures containing alkanes, carbon dioxide, and nitrogen. *AIChE J.* **2001**, *47*, 1676–1682.

(33) Levesque, D.; Gicquel, A.; Darkrim, F. L. and Kayiran, S. B., Monte Carlo simulations of hydrogen storage in carbon nanotubes, *J. Phys.: Condens. Matter* **2002**, *14*, 9285–9293.

(34) Smith, W.; Yong, C. W.; Rodger, P. M. DL_POLY: Application to molecular simulation. *Mol. Simul.* **2002**, *28*, 385–471.

(35) Jelfs, K. E.; Eden, E.; Culshaw, J. L.; Shakespeare, S.; Pyzer-Knapp, E. O.; Thompson, H. P. G.; Bacsza, J.; Day, G. M.; Adams, D. J.; Cooper, A. I. In silico design of supramolecules from their precursors: odd–even effects in cage-forming reactions. *J. Am. Chem. Soc.* **2013**, *135*, 9307–9310.

(36) Vitillo, J.; Ricchiardi, G.; Spoto, G.; Zecchina, A. Theoretical maximal storage of hydrogen in zeolitic frameworks. *2005*, *7*, 3948–3954.

(37) Li, W.; Grimme, S.; Krieg, H.; Möllmann, J.; Zhang, J. Accurate computation of gas uptake in microporous organic molecular crystals. *J. Phys. Chem. C* **2012**, *116*, 8865–8871.
Hasell, T.; Armstrong, J. A.; Jelfs, K. E.; Tay, F. H.; Thomas, K. M.; Kazarian, S. G.; Cooper, A. I. High-pressure carbon dioxide uptake for porous organic cages: comparison of spectroscopic and manometric measurement techniques. *Chem. Commun.* **2013**, *49*, 9410–9412.

Chen, L.; Reiss, P. S.; Chong, S. Y.; Holden, D.; Jelfs, K. E. Separation of rare gases and chiral molecules by selective binding in porous organic cages. *Nat. Mater.* **2014**, *13*, 954-960.

Tozawa, T.; Jones, J. T. A.; Swamy, S. I.; Jiang, S.; Adams, D. J.; Shakespeare, S.; Bradshaw, D.; Hasell, T.; Chong, S. Y.; Tang, C.; et al. Porous organic cages. *Nat. Mater.* **2009**, *8*, 973–978.

Lee, T.-C.; Kalenius, E.; Lazar, A. I.; Assaf, K. I.; Kuhnert, N.; Grün, C. H.; Jänis, J.; Scherman, O. A.; Nau, W. M. Chemistry inside molecular containers in the gas phase. *Nature Chem.* **2013**, *5*, 376-382.

Brutschy, M.; Schneider, M. W.; Mastalerz, M.; Waldvogel, S. R. Porous organic cage compounds as highly potent affinity materials for sensing by quartz crystal microbalances. *Adv. Mater.* **2012**, *24*, 6049–6052.

Acharyya, K.; Mukherjee, P. S. A fluorescent organic cage for picric acid detection. *Chem. Commun.* **2014**, *50*, 15788.
