

Ionic clusters as high-connectivity secondary building units for crystalline porous organic salts

Corresponding Author: Professor Andrew Ian Cooper

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Comments for the Author)

In their work "Non-metal ionic clusters as 'soft' high-connectivity secondary building units for crystalline porous organic salts", Lu and colleagues use the ammonium halides, known for their ability to construct porous materials via Coulombic attraction, and extend the concept to a broader (and hard to control) range of N_mX_n ionic clusters to construct porous materials, increasing diversity from the known examples using N_4X_4 . The work is overall of high quality, and brings novelty in a direction rarely explored.

The authors show the effect of different clusters on the resulting structural diversity, but there is a lack of systematic topology analysis and rationalization of the findings, which would have given another dimension to the work, and would have helped avoid potentially misleading structural analogies. Especially, the abstract suggests that the targeted challenge is "to design and realise porous crystalline packings with the highly connected reticular topologies that can be achieved in MOFs." While the word "design" can be interpreted in various ways (structural predictability is not achieved here), topologies should nevertheless be analyzed and described with sufficient detail, allowing comparison/analogies with MOFs, COFs and other reticular materials:

-The authors should give their description of what an SBU is in this context. Is it a cluster, chemical entity as in Figure 1a (which displays non-existing Zr-Zr bonds, on a side note), or a purely geometrical entity, as in Figure 1d? Figure 2e-g seem to show hybrid of the two, and would benefit from more consistency.

-The reported (4,4)-c, (6,6)-c, and (6,12)-c networks are not analyzed against known nets (e.g. from RCSR, EPINET...). It therefore remains unclear what these topologies are, and whether they are common, rare, or maybe even new. Similarly, the analogy drawn to NU-1500 (line 274) reflects a perception from the authors but is likely inaccurate; a proper topological assignment (potentially nia, like in NU-1600 rather than acs in NU-1500) is required to drive the discussion on facts more than perception.

-The definition and representation of building units do bring some ambiguity. The manuscript would benefit from explicitly distinguishing between cluster geometry and points of extension, which govern topology. For instance, N_4Cl_4 is represented as a cuboid, and its connectivity corresponds to a tetrahedral node, or a tetrahedron. The description of the $N_{12}Cl_7$ cluster is particularly confusing; the green polyhedron described as a hexagonal prism excludes six N atoms from the cluster, therefore highlighting a N_6Cl_7 fragment with unclear interest/utility. Then, six additional N (part of the cluster formula) are considered, bringing the connectivity to 12. However, no corresponding topological representation of the vertex figure/directionality is given, despite its impact on the resulting structure. For $N_{12}Cl_9$, in addition to a complete cluster shape and corresponding topology vertex figure, the choice of distance cutoff (3.4 Å) needs further explanation. Figure 1f suggests a more natural cutoff at 3.3 Å (which would then change the nature of the cluster and decrease ligand connectivity), while extending to 3.5 Å would then result in an infinite array.

-The authors successfully use typical reticular chemistry tweaks to increase structural diversity, and while they spend some time explaining the effect of methyl groups on the resulting ligand geometry, it would add a lot if they rationalize the effect of such distortion on the resulting topology and potential structure predictability. Do the clusters remain unchanged or are they "forced" to evolve due to some geometry mismatch? etc.

-In light of the connectivity and directionality of the ionic clusters obtained in this study, and given the design challenge

mentioned in the abstract, an attempt on enumerating further topological opportunities was expected, and is surely something the readers will appreciate and value. For example, "A" topology has been achieved with this "X" cluster and ligand combination, but this cluster/building block is also compatible with "B", "C" topologies using other ligand geometries/connectivities. This could be in the form of an intuitive graphical summary table.

-L141: this statement is not easy to understand and contains some contradiction, and the authors should probably better explained what they mean by: "Ditopic and tritopic organic linkers can only provide planar or pyramidal directionality rather than a 3D spatial arrangement." Pyramidal directionality is clearly non planar, and therefore 3D. Meanwhile, 4-connected can also be flat. The position of the linking group in ortho, meta or para from the central core, as well as the introduction of steric hindrance are also known to have a major impact on resulting dimensionality and spatial arrangement. To make an analogy with MOFs, there are many 3D MOFs made out of ditopic ligands and tritopic ligands, and also a non-negligible number of 2D MOFs with 4-c linkers.

While I do not believe properties are a must in such type of work, it is pretty interesting and inspiring to see the effect/impact of non evacuated solvent on porosity, including H₂ uptake. As a curiosity, have the authors tried some high pressure sorption to see whether in some cases, solvent can be replaced by gas molecules without structural collapse?

Typically, N₂ isotherms are plotted in cm³/g, and H₂ uptake is evaluated in weight %. While the current choice of having all uptakes in mmol/g is correct, providing isotherms with the most used units would help reader better contextualize the uptakes and potential performances.

Overall, this work is a promising and original contribution which would benefit from more consistency as well as a rigorous improvement on the structural and topological description aspects, and from a discussion about the resulting reticular design perspective. With these enhancements, this paper will be truly useful to the reticular chemistry community, and beyond, for the readers who will better appreciate the significance of the opportunities brought by these achievements.

I support transparent peer review.
Vincent Guillermin

Reviewer #2

(Comments for the Author)

The manuscript by Fellowes, Cooper and co-workers describes a new approach to preparing a series of hydrogen-bonded organic frameworks (HOFs). This is primarily a crystal engineering study, and some beautiful crystal structures are obtained. To my mind, the key advance is the demonstration that organic ammonium cations and halide anions can form large clusters reminiscent of secondary building units (sbu) that are so fundamental in the MOF literature. At the moment, the materials properties of the resulting frameworks are interesting but not hugely remarkable. There is some literature precedence for smaller ammonium-anion clusters both in the authors previous work in this area (references 12-14) and the work of Tohnai (reference 25, and earlier work by this group).

The manuscript is clearly-written, well-presented and the experimental studies are carried out to a very high standard. The X-ray crystallography appears to have been conducted very well.

I'm on the fence as to whether this advance is sufficiently novel or broad in scope to justify publication in Nature Chemistry. The key utility of MOF sbu is that they form reproducibly across a wide range of systems, where the current manuscript reports only one example of each of the large clusters. If the authors could show that they can access some of these clusters from different poly-ammonium derivatives I think that would certainly increase the broad appeal, although I appreciate this might be a lot of work. I leave it up to the editor and other referees whether they think the work is novel enough for Nature Chemistry, but if not I think after some revisions this would make for a nice paper somewhere like J. Am. Chem. Soc. or Nat. Commun.

Suggested clarifications:

- The authors refer to "non-metal ionic clusters" and "non-metal organic frameworks." This naming feels like a joke name given to the frameworks in the lab, which has somehow made it into the scientific literature. In my opinion the "non-metal organic X" naming is so broad as to be meaningless. Presumably the overwhelming majority of covalent organic frameworks and hydrogen-bonded organic frameworks are also "non-metal organic frameworks," and any organic salt is a "non-metal ionic cluster." I know the authors have published a few recent papers using this terminology, possibly because reviewers thought it was funny, but I think this is really unhelpfully vague. "Ammonium halide frameworks" would be much clearer in my opinion.

- I found the discussion of crystallisation solvents quite confusing. The authors state the nature of the solvent is important and at line 156 describe using methanol as crystallisation solvent. At later points they refer to e.g. "crystallisation from THF or EtOAc" (line 203) or "crystallisation...carried out in acetonitrile, ethyl acetate or diethyl ether" (line 209). The Methods section clarifies this (I think) by noting that crystallisation was carried out from methanol/DMF with an anti-solvent. I think the wording could do to be clarified throughout, and it would be good to mention that the methanol contained some DMF when this is first discussed.

Other suggested changes:

Line 49: The authors say that the ligands in NU-1000 and PCN-224 "favour dense packing." I'm not quite sure what the

authors mean by this. The carboxylate groups in these MOFs point away from one another?

Line 55/56: "such as hydrogen-bonded organic frameworks (HOFs) and crystalline porous organic salts (CPOS)." I think CPOS are a subset of HOFs rather than a separate class of materials.

Line 60/61: The authors state that HOFs tend to be 2D rather than 3D structures. I disagree with this, there are lots and lots of 3D HOFs.

Line 144: I don't think it's useful to include the IUPAC name of TAHP. At least to me, a name this long is completely unintelligible.

Line 229: I don't think it makes sense to give a calculated value to 5 significant figures (-117.11 kJ/mol). There is no way the value is known this accurately.

Line 270: Missing word in "and chloroform the antisolvent."

Line 323: I don't think it makes sense to give an amount of solvent calculated from NMR integration to 4 significant figures ("13.52%").

Lines 345-347: I don't think having two solvent molecules in a cavity is particularly unusual, and I am not sure it is particularly reminiscent of Yoshizawa's work. I suggest removing this sentence.

Line 370: Missing word "gives the pore size about 3.8 Å"

Figures: There is some quite small text on the axes of some of the figures throughout; it might be helpful to make this a bit bigger.

SI: typo "Bond length and angel index in CSD"

SI: The authors state that all reagents were obtained from various commercial suppliers. Is this true for hexabromotriptycene and the tetraiodobiphenyl compound? If not, could references for how these were made be provided?

SI: The authors refer to "degassing" with bubbling N₂. I'm not sure adding gas to something degasses it? Perhaps "deoxygenating"?

SI: Caption to Supplementary Fig. 36. I don't think a pentane loading can be determined accurately to 0.01% ("13.52 wt %"). Perhaps 14% would be better here?

Reviewer #3

(Comments for the Author)

The authors present a study using coulombic forces to create porous non-metallic MOFs. The study appears to be generally well-undertaken and written.

The authors use a TAHP core as a 4-connected linker, followed by TAHPMe. In TAHPMe there are two non-equivalent methyl groups - the internal pair that dictate the dihedral angle of the linker, and the single methyl group between the two amino groups. What would be the effect of removing the 'single' methyl group?

The author should additionally specify all cage topologies (e.g. in Fig 2) using Jelfs' notation (<https://doi.org/10.1039/C7NR00703E>) and MOFs (e.g. Line 275, NU-1500i and Fig 4) using RCSR notation.

The "structural n-pentane" is interesting and needs to be discussed a bit more. There are several mentions of "exchanged for alkanes" - so what other alkanes were used, and what were the results? The picture of n-pentane@cage seems to indicate a very good structure/size fit. a) provide the coordinates (computational structures should be FAIR and treated equivalently to crystal structures) b) does the 13.52 wt% of n-pentane correspond to all cages containing a single n-pentane?

Version 1:

Reviewer comments:

Reviewer #1

(Comments for the Author)

Lu and colleagues have revised their article, now titled "Ionic clusters as 'soft' high-connectivity secondary building units for crystalline porous organic salts".

The manuscript is noticeably improved, particularly, some topology aspects were not clear (geometry, connectivity of the clusters, topology assignments, etc.) and are now described following satisfactory standards, along with some confusing parts of the figures which have also been adjusted. I believe this will help readers a lot, and be a source of inspiration for further designing "non-metal organic frameworks".

The sorption part has been revised and the plots now use more common units, which facilitates immediate understanding and comparison with other reported materials, which is always a plus.

Overall, I have the feeling the authors provided a stronger, improved version of their work, and that the findings/achievements relevance is not affected by the modifications. I do not have further comments which would not fall into the "personal preference" category (such as the points of connection not matching the SBU vertices on the schematic non-metal organic framework on the TOC image and Figure 1d), and I am looking forward to see more developments in this

direction in the coming years.

I support transparent peer review, Vincent Guillermin

Reviewer #2

(Comments for the Author)

The authors have conducted a significant number of experiments and have re-phrased the manuscript to make clarifications. The additional results showing different anions give similar structures are reassuring as I think it increases the generality of the approach. Even though these won't be published in the current work, I think it adds support to the authors' hypothesis that this is a general approach to predictable framework formation. I suggest this manuscript be accepted for publication.

Reviewer #3

(Comments for the Author)

The authors have done a respectable job of addressing my and the other reviewers' points.

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The point-by-point responses to reviewers' comments

Reviewer comments:

Reviewer #1 (Comments for the Author):

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The authors show the effect of different clusters on the resulting structural diversity, but there is a lack of systematic topology analysis and rationalization of the findings, which would have given another dimension to the work, and would have helped avoid potentially misleading structural analogies. Especially, the abstract suggests that the targeted challenge is “to design and realise porous crystalline packings with the highly connected reticular topologies that can be achieved in MOFs.” While the word “design” can be interpreted in various ways (structural predictability is not achieved here), topologies should nevertheless be analyzed and described with sufficient detail, allowing comparison/analogies with MOFs, COFs and other reticular materials:

Response: We thank the reviewer for this positive evaluation of our work. We also appreciate the valuable suggestions, which have prompted us to further interpret these structures from a topological perspective. We feel this has improved the quality and clarity of the study. In response to the reviewer's suggestion regarding topological analysis, we have revised Fig. 2 and Fig. 4 to incorporate both topological and SBU analyses. Additional details have also been included in the Supporting Information to further support these topological assignments. These revisions provide a clearer and more systematic interpretation of the reported structures and their underlying framework architectures.

-The authors should give their description of what an SBU is in this context. Is it a cluster, chemical entity as in Figure 1a (which displays non-existing Zr-Zr bonds, on a side note), or a purely geometrical entity, as in Figure 1d? Figure 2e-g seem to show hybrid of the two, and would benefit from more consistency.

Response: We thank the reviewer for this helpful suggestion regarding the presentation of the SBUs. In the revised manuscript, we have distinguished the chemical structure of the molecular building block (MBB) from the simplified SBU connectivity model used to describe its role in the framework, whereby The SBUs are defined as polyhedral assemblies, with connectivity extending from the anilinium centres (see Fig. 1d).

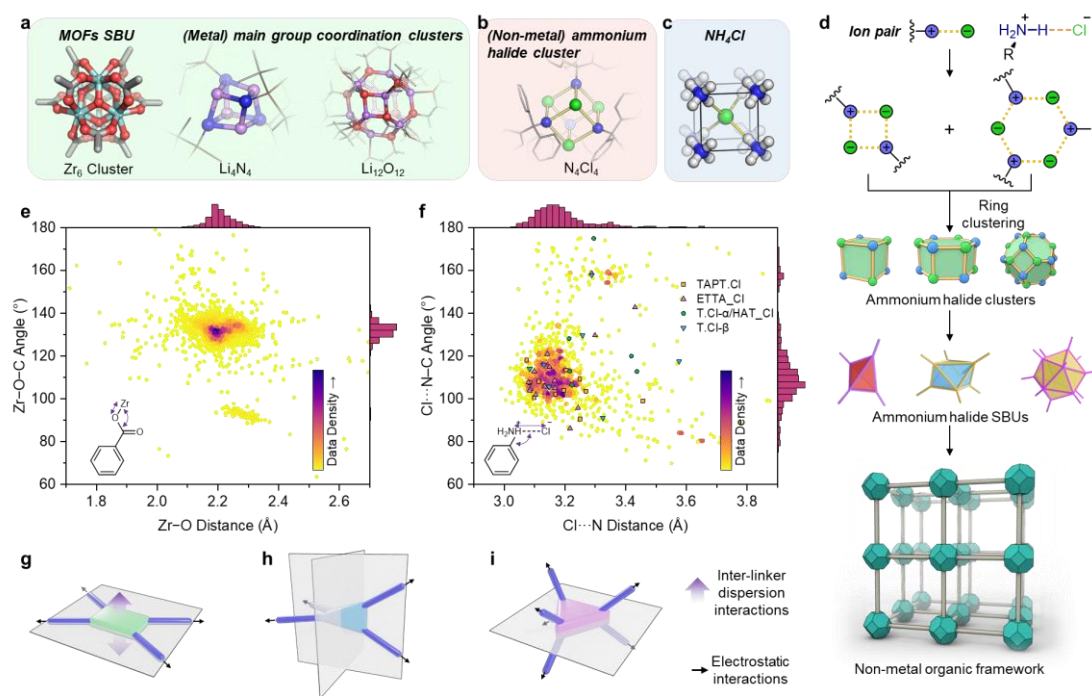


Fig. 1 | Structural design of ammonium halide SBU-based non-metal organic frameworks. **a**, Metal-based Zr_6 12-c SBU in MOFs, compared with representative main-group clusters, such as cubic Li_4N_4 and twisted truncated-octahedral $Li_{12}O_{12}$. **b**, Cubane type ammonium halide cluster. **c**, Body centred cubic structure of NH_4Cl ; the $Cl \cdots N$ distance is 3.34 Å. **d**, Ammonium halide SBUs formed from aggregated ion pairs, which further assemble into non-metal organic frameworks. The SBUs are defined as polyhedral assemblies, with connectivity extending from the anilinium centres. **e–f**, Distance and angle distributions in the Cambridge Structural Database (CSD) of carboxylate–Zr coordination bonds (**e**) and anilinium chloride ion pairs (**f**). Previously reported porous ammonium chloride frameworks are denoted by outlined symbols. **g**, Planar 4-c linker with strong interactions between linkers. **h–i**, 3D extended 4-c (**h**) and 6-c (**i**) linkers without strong interactions between linkers. Charge-bearing arms of the linkers are shown as dark-blue sticks. Neutral aromatic linker cores are represented by light-green, blue, and purple polyhedra. Electrostatic and inter-linker dispersion interactions are represented by black and light-purple arrows respectively.

We have revised Figs. 2 and 4 to show the corresponding MBBs, SBUs and simplified topological nodes for each structure. We have also revised the relevant descriptions of the clusters and SBUs in the main text. (e.g., “in which the linkers are connected by twisted-cubic N_4Cl_4 clusters. These clusters can be considered as tetrahedral 4-c SBUs”)

These changes should help clarify the distinction between the chemical species and the geometrical assemblies presented in the manuscript. In addition, we have revised the drawing in Fig. 1d for better distinguish the cluster building blocks and SBUs. Cluster structure in Fig. 1a (Zr_6) has also been revised, as suggested.

-The reported (4,4)-c, (6,6)-c, and (6,12)-c networks are not analyzed against known nets (e.g. from RCSR, EPINET...). It therefore remains unclear what these topologies are, and whether they are common, rare, or maybe even new. Similarly, the analogy drawn to NU-1500 (line 274) reflects a perception from the authors but is likely inaccurate; a proper topological assignment (potentially *nia*, like in NU-1600 rather than *acs* in NU-1500) is required to drive the discussion on facts more than perception.

Response: We thank the reviewer for this constructive suggestion. We carried out a detailed topological analysis using ToposPro and Systre, in which the geometric centres of clusters and the linkers were treated as nodes. We established the net and confirmed that (4,4)-c TAHPMe·N₄Cl₄ adopts a 2-fold interpenetrated **dia-b** net, whereas (4,12)-c TAHPMe·N₁₂Cl₁₂ exhibits the **ith** topology, which is very rare in MOFs. More notably, topological analysis of (4,12)-c TAHPMe·N₁₂Cl₇ revealed a new net, as compared against known nets in the RCSR, EPINET databases. We refer to this as **ahf** net (Fig. 2) (anilinium halide framework). In addition, as noted by the reviewer, TPA·N₆Cl₇ adopts a **nia** topology (Fig. 4 and Supplementary Fig. 37). However, because this net differs from those reported for NU-1600 and NU-1500, we have removed this comparison from the revised manuscript. We have also added corresponding sections describing the topological analysis in both the main text and the Supporting Information, for example:

*“This N₁₂Cl₇ cluster can be regarded as an SBU composed of three face-sharing trigonal antiprisms. As a result, the framework adopts a topology with the unreported point symbol of {4²¹.6⁴².8³} {4⁶}₃ in RCSR database, which we denote as the **ahf** (anilinium halide framework) net”*

“Topological analysis of TAHPMe·N₄Cl₄

*TAHPMe·N₄Cl₄ consists of 4-c TAHPMe linkers connected by 4-c N₄Cl₄ clusters. Topology simplification using ToposPro generated an initial 3-periodic net with I2/a symmetry. Subsequent symmetry enhancement in Systre increased the net symmetry to Fd-3m, and the point symbol for net was assigned as {6⁶}, allowing the structure to be assigned as a **dia** net. If the two 4-c nodes are retained as distinct node types, the corresponding binodal representation is **dia-b**.”*

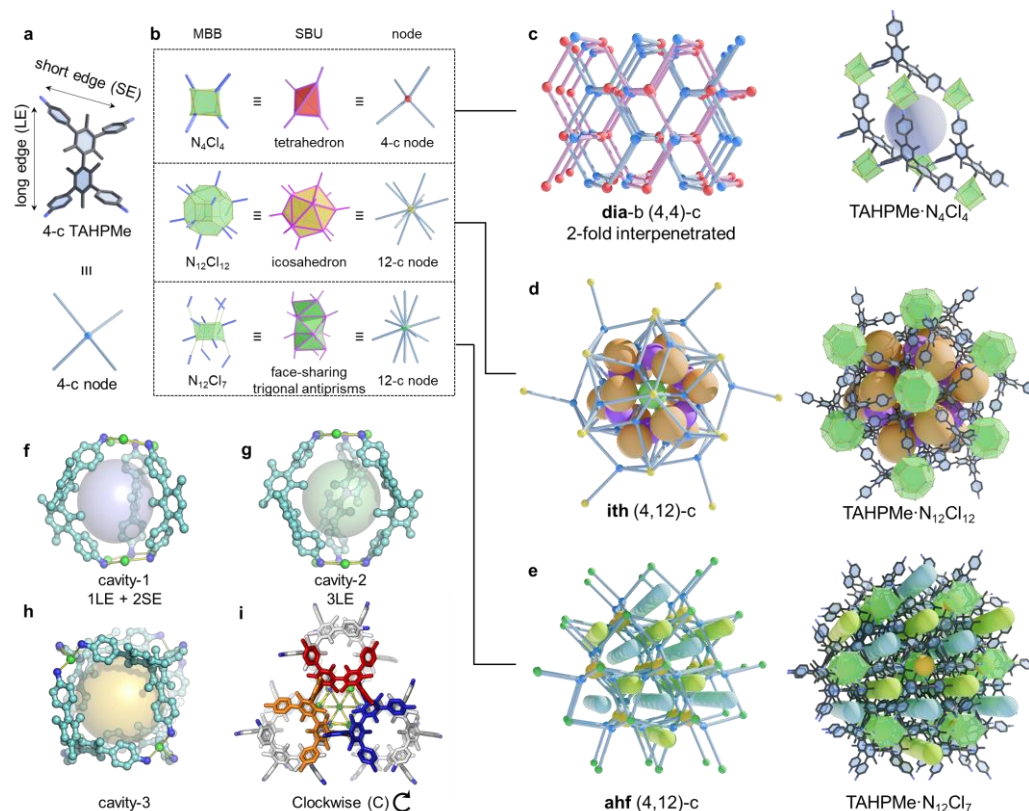
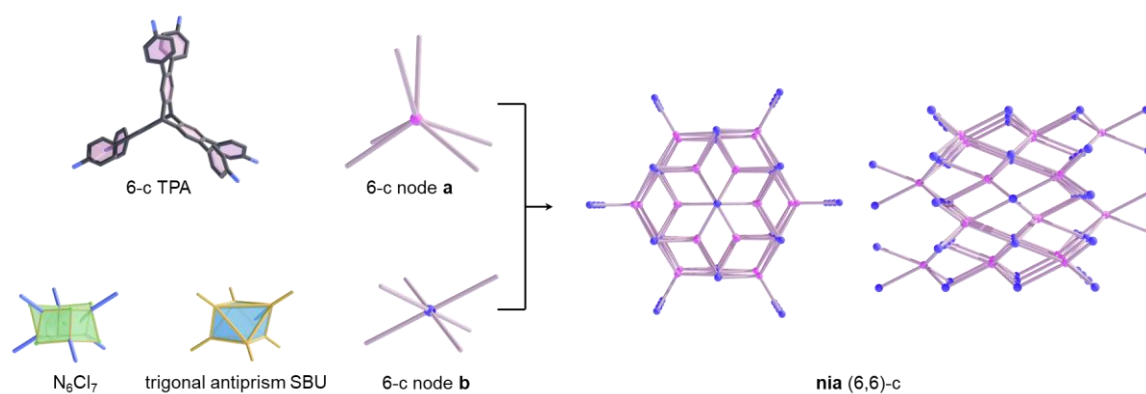


Fig. 2 | Non-metal organic frameworks assembled from a 3D directional 4-c linker, TAHPMe. **a**, Twisted TAHPMe linker showing its long and short edges, and its representation as a 4-c node in the net. **b**, Molecular building blocks (MBBs) together with the corresponding secondary building units (SBUs) and node connectivities. The SBU geometries were defined using the carbon atoms directly bonded to the NH_2/NH_3 groups as the points of extension. **c–e**, Topological representations and structures of two-fold interpenetrated **dia-b** (4,4)-c $\text{TAHPMe} \cdot \text{N}_4\text{Cl}_4$ (**c**), **ith** (4,12)-c $\text{TAHPMe} \cdot \text{N}_{12}\text{Cl}_{12}$ (**d**) and **ahf** (4,12)-c $\text{TAHPMe} \cdot \text{N}_{12}\text{Cl}_7$ (**e**). **f–h**, Cage-like structures of cavity-1 (**f**), cavity-2 (**g**), and cavity-3 (**h**) observed in $\text{TAHPMe} \cdot \text{N}_{12}\text{Cl}_{12}$. **i**, Clockwise packing of achiral TAHPMe linkers that generates the chiral centre in $\text{TAHPMe} \cdot \text{N}_{12}\text{Cl}_7$.



Supplementary Fig. 37. Topological representation of $\text{TPA} \cdot \text{N}_6\text{Cl}_7$.

-The definition and representation of building units do bring some ambiguity. The manuscript would benefit from explicitly distinguishing between cluster geometry and points of extension, which govern topology. For instance, N_4Cl_4 , is represented as a cuboid, and its connectivity corresponds to a tetrahedral node, or a tetrahedron. The description of the $N_{12}Cl_7$ cluster is particularly confusing; the green polyhedron described as a hexagonal prism excludes six N atoms from the cluster, therefore highlighting a N_6Cl_7 fragment with unclear interest/utility. Then, six additional N (part of the cluster formula) are considered, bringing the connectivity to 12. However, no corresponding topological representation of the vertex figure/directionality is given, despite its impact on the resulting structure. For $N_{12}Cl_9$, in addition to a complete cluster shape and corresponding topology vertex figure, the choice of distance cutoff (3.4 Å) needs further explanation. Figure 1f suggests a more natural cutoff at 3.3 Å (which would then change the nature of the cluster and decrease ligand connectivity), while extending to 3.5 Å would then result in an infinite array.

Response: In the revised version, we have clarified cluster geometry and points of extension in the manuscript. For example:

“connected by twisted-cubic N_4Cl_4 clusters. These clusters can be treated as tetrahedral 4-c SBUs,”

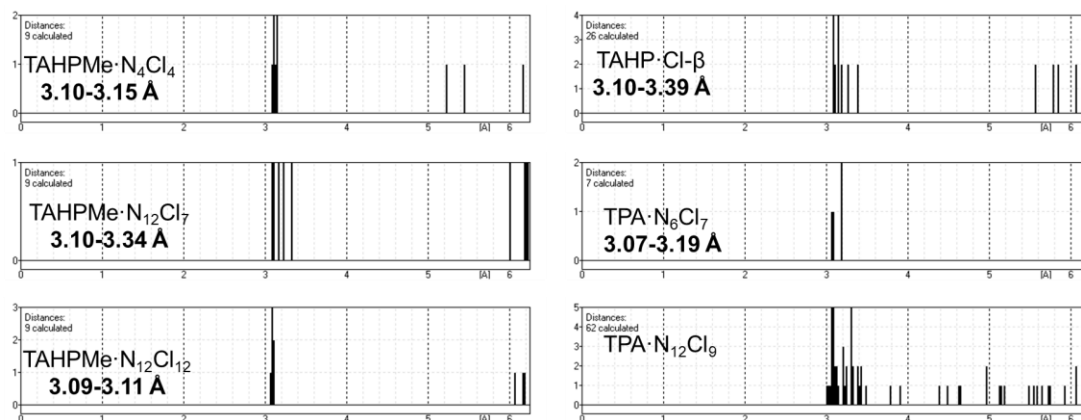
“The SBU geometries were defined using the carbon atoms directly bonded to the NH_2/NH_3 groups as the points of extension.”

Fig. 2 now separates the real chemical structures of the clusters from their connectivity as topological nodes, and the corresponding net descriptions obtained from these geometrical representations are provided in the main text and in the Supporting Information.

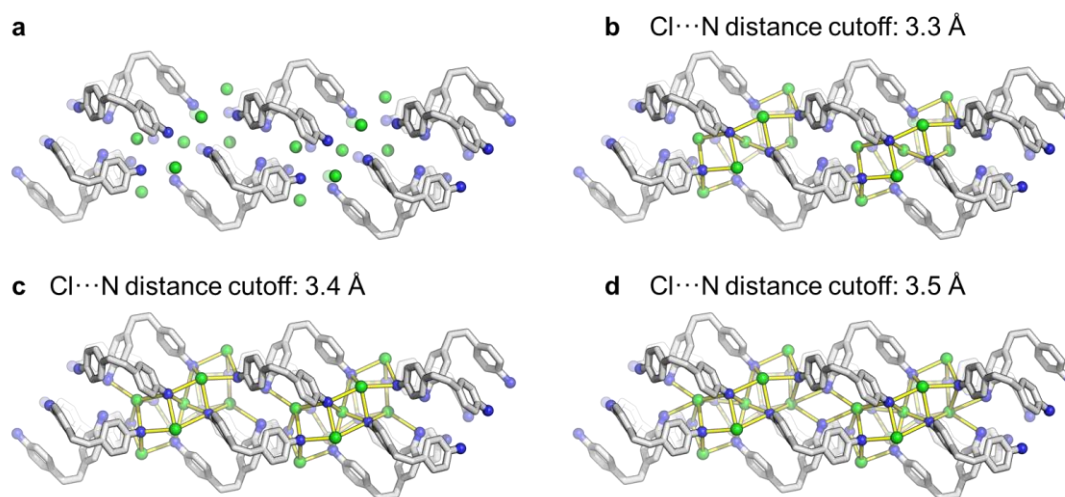
We have also revised the descriptions of the $N_{12}Cl_7$ and N_6Cl_7 clusters. The N_6Cl_7 cluster is described as a trigonal-antiprismatic 6-connected SBU, whereas the 12-connected $N_{12}Cl_7$ cluster shows a more complex face-sharing geometry derived from three trigonal antiprisms. Supplementary Fig. 27 clearly illustrates the distinction between these two cluster models in terms of both chemical structure and vertex figure.

Regarding the distance cutoff—this is an important question. We have now added a more detailed explanation in topology analysis section in Supporting Information. Although the distance distribution derived from the Cambridge Structural Database in Fig. 1f is more populated at distances below 3.3 Å, as witnessed by the higher data density in that region, the histogram above the plot in Fig. 1f suggests that a cutoff of <3.4 Å better captures the majority of $Cl \cdots N$ distances, if one takes a broad view of all reported structures. In addition, for all clusters except $TPA \cdot N_{12}Cl_9$, the $Cl \cdots N$ distance distributions show a clear separation that further supports the use of a 3.4 Å cutoff (Supplementary Fig. 32). In contrast, $TPA \cdot N_{12}Cl_9$ shows a broader $Cl \cdots N$ distance distribution, making the assignment of connectivity more subjective and small changes in the distance threshold can lead to substantial differences in the

resulting topological model. For this reason, we did not include $\text{TPA} \cdot \text{N}_{12}\text{Cl}_9$ in the topological analysis to avoid a misleading or arbitrary assignment. However, using the same 3.4 Å cutoff for the other structures allows for a clear representation of the connectivity while maintaining consistency with the N/Cl stoichiometry in the structure.



Supplementary Fig. 32. Cl $\cdots$ N distance distributions of the TAHPMe $\cdot$ N₄Cl₄, TAHPMe $\cdot$ N₁₂Cl₇, TAHPMe $\cdot$ N₁₂Cl₁₂, TAHP $\cdot$ Cl- β , TPA $\cdot$ N₆Cl₇ and TPA $\cdot$ N₁₂Cl₉.



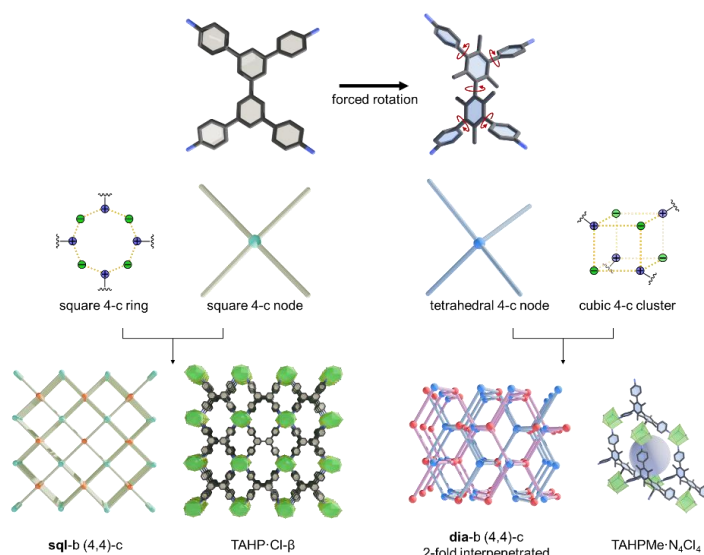
Supplementary Fig. 33. Local views of the ionic centre in $\text{TPA} \cdot \text{N}_{12}\text{Cl}_9$ using different Cl $\cdots$ N distance cutoffs to represent the ionic and hydrogen-bonding interactions.

-The authors successfully use typical reticular chemistry tweaks to increase structural diversity, and while they spend some time explaining the effect of methyl groups on the resulting ligand geometry, it would add a lot if they rationalize the effect of such distortion on the resulting topology and potential structure predictability. Do the clusters remain unchanged or are they “forced” to evolve due to some geometry mismatch? etc.

Response: We thank the reviewer for this insightful question. When the planar TAHP linker assembles with chloride anions, it forms a structurally matched ionic 4+4 cyclic centre, giving

rise to an **sql-b** topology. By contrast, methyl substitution forces the linker to distort into a tetrahedral 4-c geometry. This geometry is incompatible with the original cyclic ionic centre, and the ionic assembly therefore evolves into cluster-type nodes to accept connectivity from three-dimensional space. For example, the same 4+4 ionic composition adopts a cubic cluster geometry, enabling the formation of a **dia-b** network. The following explanation was added to the main text:

“Introducing six methyl groups onto the two central phenyl rings in the TAHP core forces the linker to distort from planar square connectivity into tetrahedral geometry. The small dihedral angle present in TAHP expands to nearly 80° in TAHPMe, which is incompatible with the original cyclic ionic centre, and the ionic assembly therefore evolves into cluster-type nodes to accept connectivity from three-dimensional space (Supplementary Figs. 16,17).”



Supplementary Fig. 17. Forced linker rotation changes the linker geometry from square to tetrahedral connectivity. This geometrical mismatch drives the transformation of the cyclic 4+4 ionic centre into cluster-type nodes, giving rise to a dia-b net.

-In light of the connectivity and directionality of the ionic clusters obtained in this study, and given the design challenge mentioned in the abstract, an attempt on enumerating further topological opportunities was expected, and is surely something the readers will appreciate and value. For example, "A" topology has been achieved with this "X" cluster and ligand combination, but this cluster/building block is also compatible with "B", "C" topologies using other ligand geometries/connectivities. This could be in the form of an intuitive graphical summary table.

Response: Following the reviewer’s suggestion, we have added information in Fig. 2 and 4 to show how different combinations of ionic clusters and topological nodes give rise to distinct framework topologies. Our work revealed that a 4-c TAHPMe linker is compatible with three distinct types of non-metal SBUs, enabling the formation of three different topological

structures. We have also added a discussion of the corresponding nodes and topological symmetry in the topology analysis section of Supporting Information:

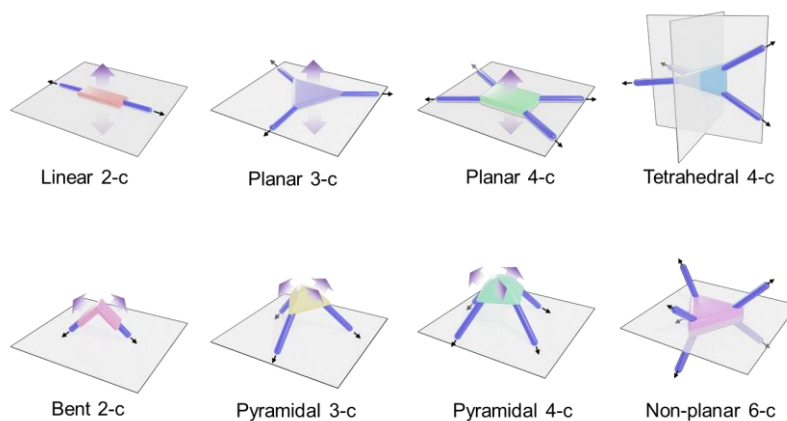
“Moreover, this type of 4-c linker is compatible with three distinct types of non-metal SBU, enabling the formation of three different topological structures.”

-L141: this statement is not easy to understand and contains some contradiction, and the authors should probably better explained what they mean by: “Ditopic and tritopic organic linkers can only provide planar or pyramidal directionality rather than a 3D spatial arrangement.” Pyramidal directionality is clearly non planar, and therefore 3D. Meanwhile, 4-connected can also be flat. The position of the linking group in ortho, meta or para from the central core, as well as the introduction of steric hindrance are also known to have a major impact on resulting dimensionality and spatial arrangement. To make an analogy with MOFs, there are many 3D MOFs made out of ditopic ligands and tritopic ligands, and also a non-negligible number of 2D MOFs with 4-c linkers.

Response: We thank the reviewer for highlighting this. The geometry of the organic linker plays a key role in determining both the framework structure and the formation of the ionic cluster. Our original intention was to emphasise that linker geometries with more spatially distributed charge points, and a reduced tendency to form close inter-linker contacts, might be advantageous for constructing higher-connectivity ionic clusters. We have now revised the relevant discussion to make this point clearer:

“Ditopic and tritopic organic linkers typically provide linear, planar or pyramidal directionality, which can still allow close inter-linker dispersion interactions in directions that are not governed by Coulombic contacts (Supplementary Fig. 15). These interactions may compete with the intended ionic connectivity and influence the resulting framework structure. By contrast, tetratopic linkers can adopt twisted tetrahedral connectivity, distributing the primary interactions in three dimensions while reducing dispersion-driven inter-linker packing.”

In addition, we have added a summary of common linker geometries in Supplementary Fig. 15.

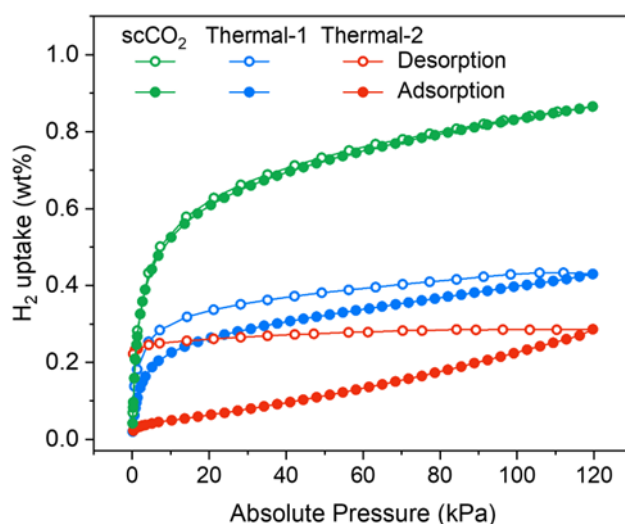


Supplementary Fig. 15. Comparison of geometric configurations between different linkers.

Charge-bearing arms of the linkers are shown as dark-blue sticks. Electrostatic and inter-linker dispersion interactions are represented by black and light-purple arrows respectively.

While I do not believe properties are a must in such type of work, it is pretty interesting and inspiring to see the effect/impact of non evacuated solvent on porosity, including H₂ uptake. As a curiosity, have the authors tried some high pressure sorption to see whether in some cases, solvent can be replaced by gas molecules without structural collapse?

Response: Owing to instrument limitations, we are not able to perform high-pressure adsorption experiments. However, comparison of different activation methods showed that residual solvent trapped within the channels substantially lowers gas uptake and gives rise to pronounced hysteresis. We have supplemented the data in Supplementary Fig. 51 as follows:



Supplementary Fig. 51. H₂ adsorption isotherms of TAHPMe·N₁₂Cl₇ obtained after different activation methods. For the thermal-1 method, the sample was exchanged with acetonitrile three times and activated directly under dynamic vacuum at 65 °C for 24 h. For the thermal-2 method, the sample was sequentially exchanged with acetonitrile, ethyl acetate and n-pentane, three times for each solvent, and then activated under dynamic vacuum at 45 °C for 24 h. Compared to the scCO₂-activated sample, incompletely activated samples exhibited lower H₂ uptake and marked hysteresis.

Typically, N₂ isotherms are plotted in cm³/g, and H₂ uptake is evaluated in weight %. While the current choice of having all uptakes in mmol/g is correct, providing isotherms with the most used units would help reader better contextualize the uptakes and potential performances.

Response: We thank the reviewer for this helpful suggestion. We have modified the plotting of these adsorption isotherms in Fig. 5 accordingly.

Overall, this work is a promising and original contribution which would benefit from more consistency as well as a rigorous improvement on the structural and topological description aspects, and from a discussion about the resulting reticular design perspective. With these enhancements, this paper will be truly useful to the reticular chemistry community, and beyond, for the readers who will better appreciate the significance of the opportunities brought by these achievements.

Response: Again, we thank the reviewer for these valuable suggestions, which feel have improved the clarity and quality of our work.

I support transparent peer review.

Vincent Guillermin

Reviewer #2 (Comments for the Author):

The manuscript by Fellowes, Cooper and co-workers describes a new approach to preparing a series of hydrogen-bonded organic frameworks (HOFs). This is primarily a crystal engineering study, and some beautiful crystal structures are obtained. To my mind, the key advance is the demonstration that organic ammonium cations and halide anions can form large clusters reminiscent of secondary building units (sbus) that are so fundamental in the MOF literature. At the moment, the materials properties of the resulting frameworks are interesting but not hugely remarkable. There is some literature precedence for smaller ammonium-anion clusters both in the authors previous work in this area (references 12-14) and the work of Tohnai (reference 25, and earlier work by this group).

The manuscript is clearly-written, well-presented and the experimental studies are carried out to a very high standard. The X-ray crystallography appears to have been conducted very well.

Response: We thank the reviewer for the positive assessment of our work. As the reviewer noted, SBU is a fundamental concept in the MOF field. The diversification of MOF topologies relies on coordination bonds between organic linkers and inorganic metal cations. This is a well-developed field, in which many structural models and basic concepts are well established. By contrast, the analogous construction of organic linkers with inorganic anions has been much less explored, let alone their use in building diverse framework structures. In this work, our intention is not simply to report new porous organic salt structures. Our aim was to provide a perspective in which non-metal ionic clusters can be considered in a manner analogous to metal-cluster SBUs, while also demonstrating a design strategy for realizing such framework structures. We believe that this viewpoint is important not only for the discovery of new framework architectures, but also for considering ionic interactions and ionic clusters to be viewed from a different perspective.

I'm on the fence as to whether this advance is sufficiently novel or broad in scope to justify publication in Nature Chemistry. The key utility of MOF sbus is that they form reproducibly

across a wide range of systems, where the current manuscript reports only one example of each of the large clusters. If the authors could show that they can access some of these clusters from different poly-ammonium derivatives I think that would certainly increase the broad appeal, although I appreciate this might be a lot of work. I leave it up to the editor and other referees whether they think the work is novel enough for Nature Chemistry, but if not I think after some revisions this would make for a nice paper somewhere like J. Am. Chem. Soc. or Nat. Commun.

Response: We understand the reviewer's concern. Unlike coordinative clusters formed through rigid coordination bonds, ionic clusters are "softer" SBUs. This suggests that the structures of the non-metal SBUs described here are dictated largely by the structural features of the linker, whereas coordination-based SBUs often arise from the intrinsic and fixed coordination geometries of metal-ligand bonding. For this reason, we believe it is reasonable that different combinations of linkers and anions can form different types of clusters, with the final structures being more sensitive to crystallization conditions. However, once a linker is shown to have the potential to form cluster structures, it might also have the potential to form alternative clusters, either with the same anion in different topologies, which we explore here, or with other types of anions. We have added the following discussion to the conclusion section to reflect this:

"Our results indicate that the formation of the "softer" ionic cluster motifs reported here is governed primarily by the structural features of the linker. Thus, once a given linker type is shown to support ionic cluster formation as an SBU, it may provide a platform for accessing other cluster architectures with different anions."

In this work, we show five types of clusters, including N_4Cl_4 , $N_{12}Cl_7$, $N_{12}Cl_{12}$, N_6Cl_7 and $N_{12}Cl_9$, obtained from two types of linkers. This supports this concept and demonstrates the feasibility of using our design strategy to construct high-connectivity clusters as SBUs for frameworks assembly.

We agree that demonstrating the same cluster across a wider range of poly-ammonium linkers would further strengthen the generality of this strategy. At this stage, our results show that once a suitable linker is identified, the ionic-cluster-forming behaviour may be extended to different anion systems.

Suggested clarifications:

- The authors refer to "non-metal ionic clusters" and "non-metal organic frameworks." This naming feels like a joke name given to the frameworks in the lab, which has somehow made it into the scientific literature. In my opinion the "non-metal organic X" naming is so broad as to be meaningless. Presumably the overwhelming majority of covalent organic frameworks and hydrogen-bonded organic frameworks are also "non-metal organic frameworks," and any organic salt is a "non-metal ionic cluster." I know the authors have published a few recent papers using this terminology, possibly because reviewers thought it was funny, but I think this is really unhelpfully vague. "Ammonium halide frameworks" would be much clearer in my opinion.

Response: Our intention here was to draw an analogy with metal–organic clusters formed through coordination interactions. In that sense, the naming is literal—these are frameworks composed entirely of non-metals; that is, (non-metal) organic frameworks, rather than ‘non-MOFs’. Moreover, as demonstrated in this study there is evidence for some level of generalisability, as in MOFs, while accepting that these are ‘softer’ SBUs (see discussion above). “Ammonium halide frameworks”, while clear, suggests that the approach is limited to halides only (see Response Fig. 1c-e). By analogy, we would not have MOFs but rather zinc organic frameworks, copper organic frameworks, etc., for each MOF-forming metal in the periodic table.

We do accept, however, that it becomes redundant and repetitious to talk about “non-metal ionic clusters”—this is implicit to the reader, and we have revised the manuscript and ESI throughout to use the simpler term “ionic clusters”.

- I found the discussion of crystallisation solvents quite confusing. The authors state the nature of the solvent is important and at line 156 describe using methanol as crystallisation solvent. At later points they refer to e.g. "crystallisation from THF or EtOAc" (line 203) or "crystallisation...carried out in acetonitrile, ethyl acetate or diethyl ether" (line 209). The Methods section clarifies this (I think) by noting that crystallisation was carried out from methanol/DMF with an anti-solvent. I think the wording could do to be clarified throughout, and it would be good to mention that the methanol contained some DMF when this is first discussed.

Response: We apologize for this lack of clarity in our original manuscript. We have now revised these sections according to the reviewer's suggestion and added the following description to the crystal-growth section:

"Stronger Coulombic attractions promote aggregation in low-polarity solvents with lower dielectric constants, which can therefore be used as antisolvents to tune the crystallization conditions. Here, a dimethylformamide/methanol/antisolvent system was used to balance the solubility of multiple species for crystallization screening."

"Crystallization from THF or 1,4-dioxane as antisolvent"

"When crystallization was carried out in acetonitrile, ethyl acetate, or diethyl ether as antisolvent,"

Other suggested changes:

Line 49: The authors say that the ligands in NU-1000 and PCN-224 "favour dense packing." I'm not quite sure what the authors mean by this. The carboxylate groups in these MOFs point away from one another?

Response: With hindsight we were insufficiently clear on this point—what we intended to convey is that these ligands tend to form close-packed structures in the absence of coordination. We have revised the sentence as follows and thank the reviewer for picking this up:

"For example, ligands with extended π systems often favour close packing in their molecular crystals through intermolecular dispersion interactions. However, in MOFs such as NU-1000 and PCN-224, the directionality and rigidity of the coordination bonds in the Zr₆ cluster prevent close packing between the ligands (Fig. 1a), thereby generating open architectures and large accessible voids."

Line 55/56: "such as hydrogen-bonded organic frameworks (HOFs) and crystalline porous organic salts (CPOS)." I think CPOS are a subset of HOFs rather than a separate class of materials.

Response: We agree that many CPOSs also contain hydrogen bonds, and both HOFs and CPOS materials are subsets of molecular frameworks. However, we referred to CPOS materials as a separate sub-category for the following reasons:

1. Both HOFs and CPOS materials contain hydrogen bonds, but ionic interactions are key for the formation and construction of CPOS structures while HOFs are typically neutral.

2. In terms of interaction strengths, hydrogen bonds are usually on the order of several to tens of kJ/mol, whereas ionic interactions are often on the order of hundreds of kJ/mol (*Chem. Soc. Rev.* **2024**, 53 (3), 1495-1513.). As such, in CPOs, the energetic contribution from hydrogen bonding accounts for a proportionately smaller part of the overall lattice energy.
3. Some porous salt materials are constructed entirely through Coulombic interactions and do not contain conventional hydrogen bonds (*J. Am. Chem. Soc.* **2023**, 145 (15), 8291-8298.). (Although we would agree that a larger number of examples do.)
4. CPO materials have charge-separated and highly polar channels. This can lead to properties that are less typical of neutral HOFs, such as proton conduction and polarization of guest molecules (*J. Am. Chem. Soc.* **2025**, 147 (18), 15429-15434.; *Angew. Chem. Int. Ed.* **2025**, 64 (31), e202509905.).

We agree with the reviewer that the ‘Venn diagrams’ for these two types of materials overlap substantially—indeed, with strong hydrogen bonding this is almost a continuum—but for the reasons outlined above, we feel that the distinction is probably worth retaining.

Line 60/61: The authors state that HOFs tend to be 2D rather than 3D structures. I disagree with this, there are lots and lots of 3D HOFs.

Response: We have rephrased this sentence as follows, which we believe is more defensible:

“For molecular crystals, the absence of high-connectivity SBUs that can link multiple linkers, together with the greater impact of weaker intermolecular interactions, can often favour simple two-dimensional (2D) packing structures or interpenetrated three-dimensional (3D) structures, rather than the more complex and diverse nets that are common in MOFs.”

Line 144: I don't think it's useful to include the IUPAC name of TAHP. At least to me, a name this long is completely unintelligible.

Response: We understand the reviewer's concern regarding readability. However, to remain consistent with the *Nature Chemistry* manuscript preparation guidelines (<https://www.nature.com/nchem/submission-guidelines/aip-and-formatting>), which recommend the use of systematic nomenclature where possible. We have retained the IUPAC name in the main text for now but we are happy to take Editorial advice on this point.

Line 229: I don't think it makes sense to give a calculated value to 5 significant figures (-117.11 kJ/mol). There is no way the value is known this accurately.

Response: We thank the reviewer for spotting this: we agree and have revised these values accordingly.

Line 270: Missing word in "and chloroform the antisolvent."

Response: This has been revised to: “and chloroform as the antisolvent”

Line 323: I don't think it makes sense to give an amount of solvent calculated from NMR integration to 4 significant figures ("13.52%").

Response: Also agreed. The calculated value has been rounded up to 14%.

Lines 345-347: I don't think having two solvent molecules in a cavity is particularly unusual, and I am not sure it is particularly reminiscent of Yoshizawa's work. I suggest removing this sentence.

Response: We have removed this sentence.

Line 370: Missing word "gives the pore size about 3.8 Å"

Response: This was a typo: we have now revised this to: "gives a pore size of about 3.8 Å"

Figures: There is some quite small text on the axes of some of the figures throughout; it might be helpful to make this a bit bigger.

Response: We thank the reviewer for this suggestion. We have carefully checked all figures and increased the font size of the smaller labels where necessary.

SI: typo "Bond length and angel index in CSD"

Response: This typo has been revised.

SI: The authors state that all reagents were obtained from various commercial suppliers. Is this true for hexabromotriptycene and the tetraiodobiphenyl compound? If not, could references for how these were made be provided?

Response: Hexabromotriptycene and tetraiodobiphenyl were obtained from commercial suppliers. We have now clarified this point in the revised SI.

"All reagents and solvents were obtained from Sigma-Aldrich, Fisher Scientific, Manchester Organics, and Alfa Aesar and used as received. 3,3',5,5'-tetraiodo-2,2',4,4',6,6'-hexamethyl-1,1'-biphenyl was obtained from Yanshen Technology Co., Ltd., and 2,3,6,7,12,13-hexabromotriptycene was obtained from BLD Pharm. TAHP was obtained from Fluorochem Limited."

SI: The authors refer to "degassing" with bubbling N₂. I'm not sure adding gas to something degasses it? Perhaps "deoxygenating"?

Response: We thank the reviewer for correcting this, we have replaced "degassing" with "deoxygenating" in the revised Supporting Information.

SI: Caption to Supplementary Fig. 36. I don't think a pentane loading can be determined accurately to 0.01% ("13.52 wt %"). Perhaps 14% would be better here?

Response: The calculated value has been revised to 14%.

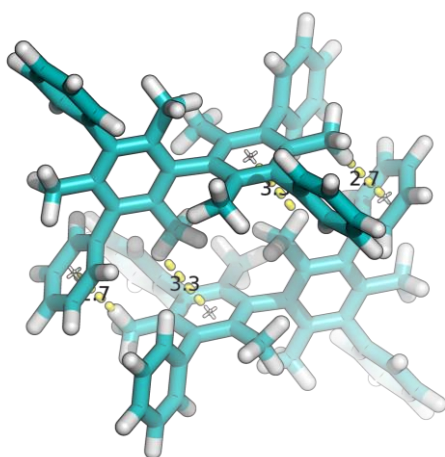
Reviewer #3 (Comments for the Author):

The authors present a study using coulombic forces to create porous non-metallic MOFs. The study appears to be generally well-undertaken and written.

The authors use a TAHP core as a 4-connected linker, followed by TAHPMe. In TAHPMe there are two non-equivalent methyl groups - the internal pair that dictate the dihedral angle of the linker, and the single methyl group between the two amino groups. What would be the effect of removing the 'single' methyl group?

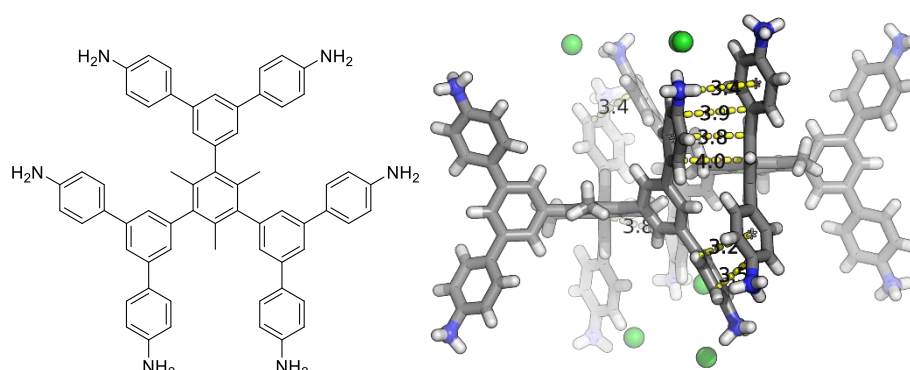
Response: We thank the reviewer for the positive comments on our work. Beyond altering the linker dihedral angle and conformation, the two non-equivalent methyl groups are important for attenuating undesired inter-linker dispersion interactions. Even in the more densely packed TAHPMe·Cl-nc structure, two types of methyl groups sterically hinder direct contacts between aromatic rings. As a result, the inter-linker dispersion interactions arise primarily from weaker contacts between the methyl groups and the aromatic rings. We have therefore added a detailed analysis of the interactions between two linker fragments in Supplementary Fig. 38:

“These weak interactions originate mostly from CH- π contacts rather than from the π - π stacking observed in TAHP, because the steric hindrance generated by the methyl groups prevents close contacts between the aromatic rings. (Fig. 3b, Supplementary Fig. 38).”



Supplementary Fig. 38. The packing of the linker fragments in TAHPMe·Cl-nc shows that two non-equivalent methyl groups provide a blocking effect that prevents close contact between the aromatic rings.

In response to the reviewer's question regarding the possible structural effect of removing one of the methyl groups, we examined the linker shown below. Although the central methyl group is sufficient to introduce steric strain and twist the linker out of planarity, the absence of the 'single' methyl group leaves the lateral aromatic arms without an effective steric group to prevent close contact between aromatic rings. This allows stronger π - π interactions between two linkers, which disfavors the assembly of a high-symmetry framework directed primarily by Coulombic interactions.



Response Fig. 2. The structure containing central methyl groups but no peripheral methyl groups, and the crystal packing mode of its chloride salt.

The author should additionally specify all cage topologies (e.g. in Fig 2) using Jelfs' notation (<https://doi.org/10.1039/C7NR00703E>) and MOFs (e.g Line 275, NU-1500i and Fig 4) using RCSR notation.

Response: We thank the reviewer for this suggestion regarding the structural description. We have supplemented the topological analysis of the obtained framework structures. We established the net and confirmed that (4,4)-c TAHPMe·N₄Cl₄ adopts a 2-fold interpenetrated **dia-b** net, whereas (4,12)-c TAHPMe·N₁₂Cl₁₂ exhibits the **ith** topology. More notably, topological analysis of (4,12)-c TAHPMe·N₁₂Cl₇ revealed a new net, against known nets in the RCSR, EPINET databases. Therefore, we refer it to as **ahf** net (Fig. 2).

Regarding the cage topologies, we note that the cage-like cavities represent local structural motifs within extended periodic frameworks rather than discrete molecular cages. We therefore consider framework net notation to be more appropriate for describing the overall topology of these materials.

The "structural *n*-pentane" is interesting and needs to be discussed a bit more. There are several mentions of "exchanged for alkanes" - so what other alkanes were used, and what were the results? The picture of *n*-pentane@ cage seems to indicate a very good structure/size fit.

Response: We thank the reviewer for their interest in this point. We first exchanged powder samples of TAHPMe·N₁₂Cl₁₂ with *n*-pentane, cyclohexane and other non-alkane solvents (Extended Data Fig. 3a). Stability tests showed that the *n*-pentane and cyclohexane exchanged samples retained crystallinity. To further investigate alkane guest binding within the framework

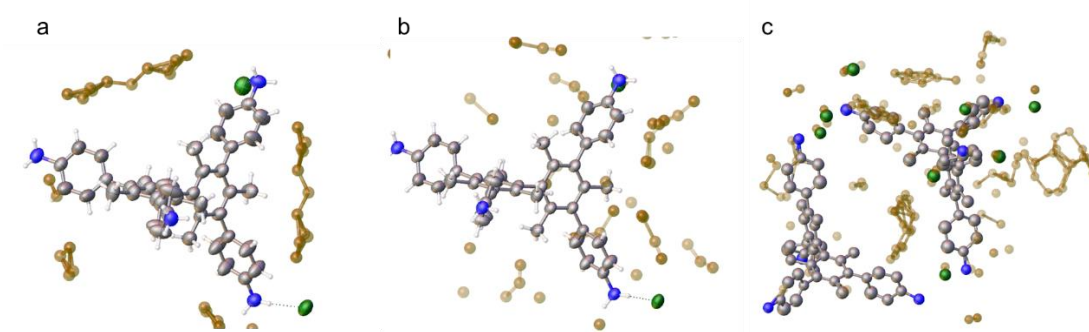
cavities, we then exchanged crystal samples with *n*-pentane, *n*-heptane, cyclohexane, methylcyclohexane and carvone. However, because of the high symmetry of the host framework, low-symmetry guests such as methylcyclohexane and carvone could not be solved unambiguously (Response Fig. 3c). In addition, smaller linear guests such as *n*-pentane do not match the cavity very well, resulting in more disordered electron density (Response Fig. 3b). For this reason, we present only the *n*-heptane@cage and cyclohexane@cage structures in the manuscript. We have now added more detailed information to the main text:

*“TAHPMe·N₁₂Cl₁₂ loses its crystallinity after direct removal of most exchanged solvent (including dichloromethane, diethyl ether, ethyl acetate, or tetrahydrofuran), while this cavity-containing framework exhibits better stability after solvent exchange with *n*-pentane or cyclohexane”*

*“To investigate the guest-binding modes within the framework, we exchanged the crystal samples with *n*-pentane, *n*-heptane, cyclohexane, methylcyclohexane and carvone. However, apart from the *n*-heptane-loaded and cyclohexane-loaded samples, the guest molecules could not be resolved unambiguously because of their disorder within the highly symmetric framework.”*

We have also added the following section to the supporting information:

*“We also investigated *n*-pentane, methylcyclohexane and carvone, in addition to the *n*-heptane and cyclohexane guests discussed in the main text. However, owing to the high symmetry of the host framework, low-symmetry guests such as methylcyclohexane and carvone could not be resolved unambiguously. Smaller linear guests such as *n*-pentane are less well matched to the cavity, resulting in more disordered electron density. In addition, the guest molecules confined within the highly symmetric cavity-2 and cavity-3 sites could not be unambiguously resolved. By contrast, guest binding could only be clearly identified at the lower-symmetry cavity-1 sites for *n*-heptane and cyclohexane.”*



Response Fig. 3. Crystal structures with unresolved guest molecules for (a) *n*-heptane@TAHPMe·N₁₂Cl₁₂, (b) *n*-pentane@TAHPMe·N₁₂Cl₁₂, and (c) carvone@TAHPMe·N₁₂Cl₁₂. The *n*-pentane- and carvone-containing structures show highly disordered Q peaks, and the guests cannot be reliably modelled. *n*-heptane contained structure shows clear Q peaks for guest assign.

- a) provide the coordinates (computational structures should be FAIR and treated equivalently to crystal structures)

Response: All coordinates of the computational structures have been included at the end of the supporting information.

b) does the 13.52 wt% of *n*-pentane correspond to all cages containing a single *n*-pentane?

Response: TAHPMe linker, cavity-1, cavity-2, and cavity-3 are present in a ratio of 3:3:1:3 in the crystal structure; therefore, one TAHPMe corresponds to 2.33 (7/3) cavities. The NMR integration shows that the ratio of TAHPMe to *n*-pentane is 1:1.7. Therefore, not all cage structures contain a single *n*-pentane molecule. We show in Supplementary Fig. 48 that *n*-pentane is still slowly released from TAHPMe·N₁₂Cl₁₂, indicating that the cage-like cavities cannot fully retain all of the *n*-pentane.