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Dodecaamide Cages: Organic 12-Arm Building Blocks for Supramolecular Chemistry

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Supporting Information

ABSTRACT: A simple, one-step amidation reaction is used to produce a range of 12-arm organic building blocks for supramolecular chemistry via the derivatization of porous imine cages. As an example, microporous dendrimers are prepared.

There has been much recent interest in the synthesis of porous organic molecules—that is, molecules that pack in either the crystalline or amorphous state to generate permanent microporosity.[1−6] Unlike extended systems such as metal−organic frameworks (MOFs)[7] or porous polymer networks,[8] there are no covalent or coordination bonds between the constituent organic building blocks. Instead, porosity arises from intrinsic porosity within the molecules, for example in porous cages, or from extrinsic porosity between the molecules, either as a result of inefficient packing[9] or programmed supramolecular assembly.[10] Compared to network or framework structures, porous molecular solids have possible processing advantages because they can be soluble in common solvents.[11,12] A range of "porous organic molecules" has been reported including imine-based cages,[13−22] diyne cages,[23] calixarenes,[24] phthalocyanines,[25] and dipeptides.[26−28] Also, by combining design strategies for polymers of intrinsic porosity (PIMs)[6,29] and conjugated microporous polymers (CMPs),[30,31] we showed recently that polyhedral oligomeric silsequioxane (POSS)-based pyrene dendrimers are microporous.[32] So far, the range of "porous molecules" is relatively narrow, and the introduction of new chemical functionality is an important goal for the future. In this regard, imine cages[13−22] might have limitations both in terms of physicochemical stability (though some are quite stable)[33] and in their scope for further synthetic elaboration. Thus, it is valuable to explore new routes to functional derivatives of organic cage molecules, both in the context of porous solids and, more generally, as new supramolecular building blocks.

Here, we show that imine cages can be converted, in a synthetically generalizable approach, into robust dodecaamide cages via reduction to an amine cage intermediate. As well as giving microporous materials in some cases, the method provides a simple and versatile two-step route to a wide range of organic building blocks via the introduction of 12 functional arms around a small (∼2 nm) organic core.

We reported previously the synthesis of a crystalline cage, **CC1** (Figure 1), via the [4+6] imine condensation of 1,3,5-triformylbenzene with 1,2-diaminoethane.[13] We have also demonstrated reduction of this imine cage to the corresponding amine, **RCC1**, using sodium borohydride.[34]

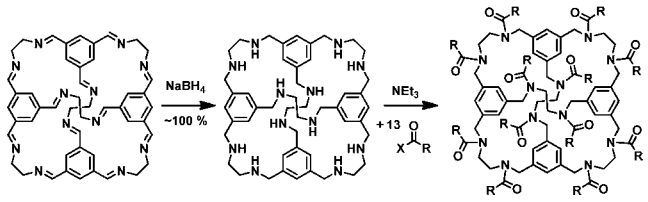

Figure 1. Synthesis of dodecaamide cages from organic imine cage **CC1** via reduction to an amine cage, **RCC1**.

We used this reduced amine cage, for example, as a "pre-porous" linker in a MOF.[34] Also, post-modification of hydroxyl-functionalized cages by Williamson etherification was used previously by Mastalerz.[35] Here, we show that simple reaction of acid halides with the amine groups in **RCC1** can be used to form a range of dodecaamide organic cages.

As examples of functional groups, we chose 4-bromobenzoyl chloride, 2-naphthoyl chloride, 1-adamantanecarbonyl chloride, and 2-bromoisobutyryl bromide to give dodecaamide cages **RCC1a**, **RCC1b**, **RCC1c**, and **RCC1d**, respectively, although we have preliminary evidence that this route is quite generalizable to other functionalities such as long-chain aliphatic chains and pyridine. 2-Naphthoyl chloride and 1-adamantanecarbonyl chloride were chosen to show that we could post-synthetically modify all 12 amines in the rather compact core of **RCC1** with relatively bulky functional groups. 4-Bromobenzoyl chloride and 2-bromoisobutyryl bromide were selected because of their potential for further synthetic modification, either via metal-catalyzed coupling reactions or, in the latter case, to create a possible 12-arm amide cage initiator for atom transfer radical polymerization (ATRP).

In all cases, the reactions were found to proceed effectively to the target dodecaamide cages with evidence for complete amidation of all 12 amines in **RCC1**. A slight (5%) excess of acid halide was used in the presence of triethylamine to ensure complete conversion. Purification of the crude mixture was carried out by column chromatography to give the functionalized cages in final isolated yields of around 50%. The structures of the functionalized cages were verified by ^{1}H and ^{13}C NMR and MALDI-TOF (see Supporting Information, Figures S1−S13). The signals in the NMR were relatively

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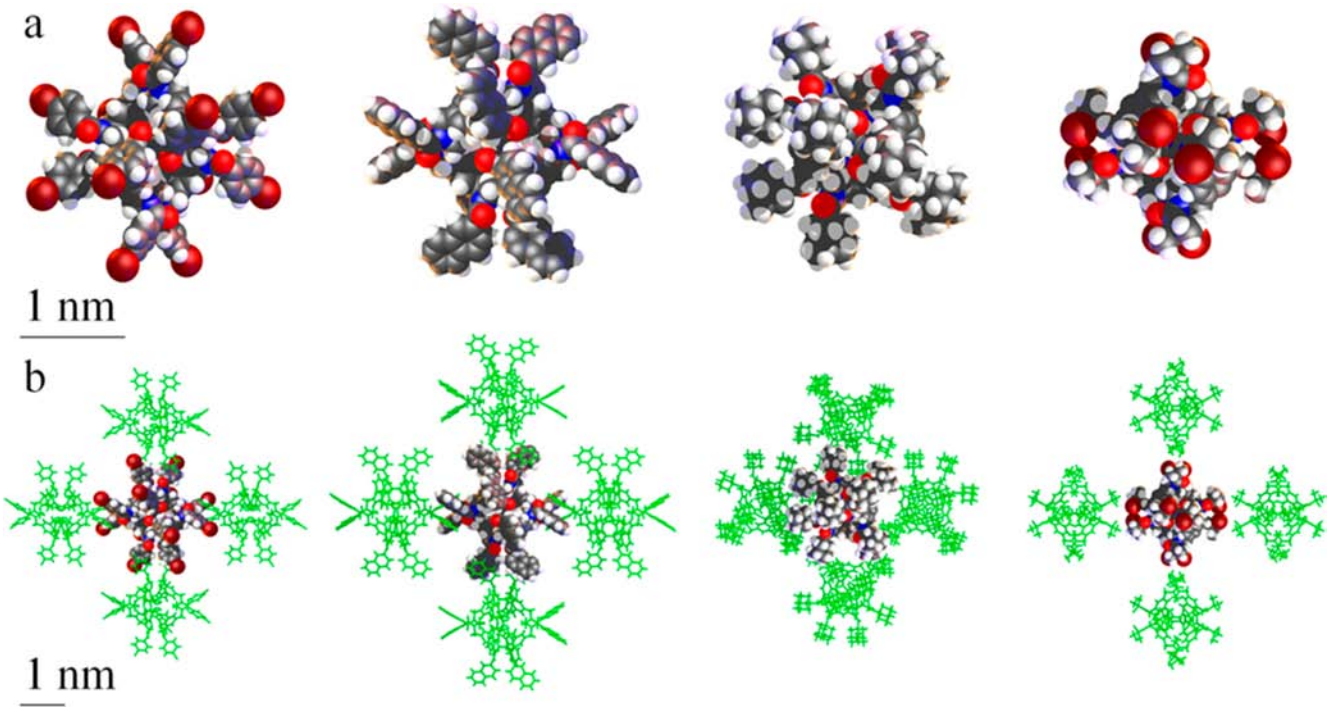

Figure 2. (a) Single-crystal X-ray structures of (left to right) **RCC1a**, **RCC1b**, **RCC1c**, and **RCC1d** in space-filling representation showing individual dodecaamide cages. (b) Packing diagrams of **RCC1a**, **RCC1b**, **RCC1c**, and **RCC1d** (solvent molecules not shown).

broad, which we rationalize on the basis of the many rotamers present in each amide-functionalized cage, resulting in a series of positional isomers (note that amide bonds do not allow free rotation). MALDI-TOF showed the presence of the expected dodecaamide cage, with no evidence of lower degrees of functionalization.

After purification, crystals of each of the dodecaamide cages were grown via layering with various solvent mixtures. The structures derived from single-crystal X-ray diffraction (SCXRD) are shown in Figure 2. For SCXRD analysis, the crystals were removed from solution and placed immediately in protective oil before mounting at 100 K on the diffractometer. When exposing the crystals to air at ambient temperatures, **RCC1a**, **RCC1c**, and **RCC1d** rapidly lose their solvent content and become X-ray amorphous in the process. Only single crystals of **RCC1b** were stable in air under these conditions. Some of the solvent molecules ($CHCl_3$) in **RCC1b** and **RCC1c** are heavily disordered, but positions were refined where possible. The largest solvent-free void that is large enough, in principle, to accommodate solvent was found for **RCC1c** (~100 Å^3), located in the centers of the cages. The largest solvent-accessible void in **RCC1d** was smaller than 25 Å^3, and no voids were found in either **RCC1a** or **RCC1b**. We are therefore confident that we have located the majority of solvent molecules, and empirical formulas for the solvates are based on these structure refinements (Supporting Information).

RCC1a, **RCC1b**, and **RCC1d** crystallize with cubic symmetry, and all show similar packing motifs (Figure 2b). The pendant aromatic bromophenyl and naphthyl groups in **RCC1a** and **RCC1b** form intercalating $\pi-\pi$ interactions with neighboring cage molecules to give three-dimensional interconnected networks (Figure 2b shows 2-D slices for clarity). In addition to the $\pi-\pi$ stacks, **RCC1b** (but not **RCC1a**) shows further C−H···π interactions between molecules located in neighboring layers of the 3-D structure. This, and the greater electronic overlap between the naphthyl groups compared to phenyl groups, might explain why **RCC1b** retains its crystalline structure to significantly higher temperatures than **RCC1a**.

The molecular packing in **RCC1d** is similar to that of **RCC1a** and **RCC1b**, but here the cage−cage intermolecular interactions consist only of weak C−H···Br contacts, and the dominant intermolecular motifs are C−H···O interactions involving the chloroform solvent molecules, which, of course, are removed upon desolvation, contributing to the structural instability of this solvate. The same is true for **RCC1c**, which crystallizes with tetragonal symmetry. In this case, the cage is decorated by adamantane groups that offer little directing functionality in terms of intermolecular cage−cage interactions. Also, the solvent content in **RCC1c** and **RCC1d** (~46−48% of the unit cell volume) is considerably higher than for the solvates of **RCC1a** and **RCC1b** (~28−30%), increasing the likelihood of amorphization upon desolvation.

After desolvation, which renders the samples amorphous, **RCC1a**−**RCC1d** were found to be non-porous to both nitrogen and hydrogen at 77 K. However, this synthetic methodology also allowed us to prepare 12-arm dendrimers around a tight, compact organic core via a convergent route.[36] An inorganic−organic analogy is the well-known series of polyhedral oligomeric silsesquioxane (POSS) molecules, where 8-arm dendrimers have been prepared, for example, from octafunctional-POSS.[37] Dodecafunctional-POSS has also been reported, but this unit has a lower symmetry compared to the cages reported here.[38,39] Our cages are effectively truncated tetrahedra (Figure S13), with four triangular and four hexagonal faces. By contrast, dodecafunctional-POSS has four pentagonal and four square faces.[39] Another molecule that has 12 functionalizable positions is coronene,[40] but again this has a very different, disk-like shape. Other dendrimers with 12 arms have a substantially lower spatial functional group density

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compared with these amide-cage molecules.[41] There are also analogies here with substituted C_{60}.[42,43]

We recently reported two POSS-based dendrimers that showed permanent microporosity in the solid, amorphous state.[32] The larger of these two POSS dendrimers showed the highest level of porosity. Here, we prepared large, rigid, 12-arm dendrimers from **RCC1** (Figure 3). First, we synthesized the

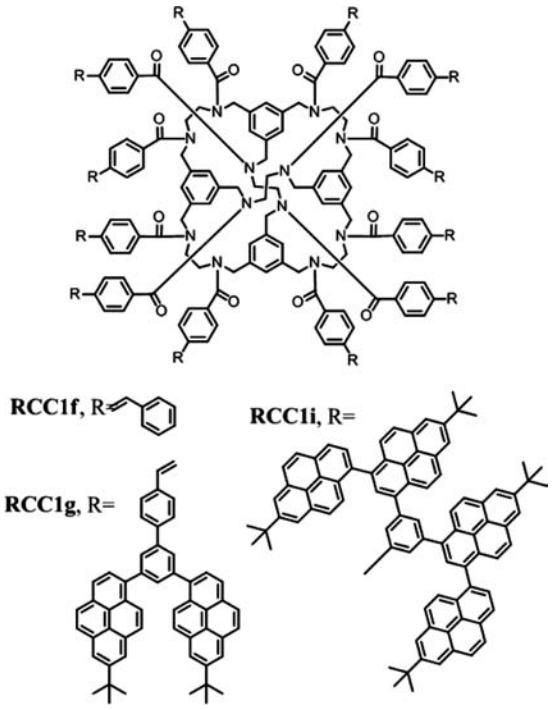

Figure 3. Structures of 12-arm dendrimers **RCC1f**, **RCC1g**, and **RCC1i**. For full structures and syntheses, see Scheme S1 in the Supporting Information.

iodo-analogue of **RCC1a**, via reaction of **RCC1** with 4-iodobenzoylchloride to give **RCC1e**. Reaction with styrene, catalyzed by palladium acetate, afforded dendrimer **RCC1f**. Similarly, the palladium catalyzed reaction with a pyrene-based dendron (Figure 3) afforded **RCC1g** in 28% yield. A larger dendrimer was synthesized by first reacting **RCC1e** with 3,5-dibromophenylboronic acid to give **RCC1h**. The resulting dendrimer was then reacted with the pyrene-based dendron to give **RCC1i** in a 46% yield.

As expected, gel permeation chromatography (GPC) demonstrated that the molecular weight distribution for each dendrimer was monodisperse (M_w/M_n < 1.03, see Figure S14). We were unable to obtain MALDI-TOF data for **RCC1g** and **RCC1i** to confirm total substitution, but the monodispersity of the GPC data suggests that a single molecule is formed, as opposed a mixture of substitution levels. Following the protocols we developed for our POSS-based dendrimers, each of **RCC1f**, **RCC1g**, and **RCC1i** was dissolved in dichloromethane and then precipitated into methanol to afford a solid powder. The porosity of the resulting precipitated dendrimers was then measured (Table 1).

RCC1f and **RCC1g** show low porosity to nitrogen at 77 K, but the larger dendrimer, **RCC1i**, was significantly more porous, with an apparent Brunauer–Emmett–Teller surface area (SA_{BET}) of 252 m^2/g. The material is also porous to both hydrogen and carbon dioxide, which suggests potential for use

Table 1. Molecular Weight and Sorption Data for Dendrimers

dendrimer	M_w (g/mol)	M_n (g/mol)	PDI	SA_{BET} (m^2/g)[a]
RCC1e	508	475	1.07	*b*
RCC1f	2465	2414	1.02	41
RCC1g	6110	5948	1.03	93
RCC1i	5981	5822	1.03	252

[a]Apparent BET surface area calculated over the range P/P_0 = 0.01–0.1. [b]Not determined.

as a "soluble porous additive" in macroporous supports,[12] or perhaps as a soluble organic component to be blended with other porous polymers, such as PIMs[11] (Figures S16–S19). As we suggested for POSS-based dendrimers,[32] we hypothesize that the larger dendrimer here is significantly less interpenetrated in the bulk as a result of the number of pyrene groups, resulting in an enhancement in microporosity. These "porous molecules" are also chemically robust: for example, the dendrimers can be boiled overnight in NaOH (pH 12) without any sign of decomposition. While the level of porosity in these dendrimers is too low for applications such as gas storage, large surface areas and pore volumes are not necessarily a requirement for selective gas separations. As such, the combination of porosity, solution processability, and chemical robustness suggests potential for the formation of thin-film gas separation membranes.[6,29]

In conclusion, the dodecamine cage **RCC1** is a versatile platform for 12-arm molecules with a compact structure and a high functional group density (for example, RCC1c has an "inclusion sphere radius" of only 11.74 Å and an associated inclusion sphere volume of 6785.1 $Å^3$, see Figure S20). Small organic molecules with as many as 12 functional groups are quite rare, but here we show that facile reaction with an acid halide allows complete conversion to a range of dodecaamide materials which are potential building blocks in both crystalline and amorphous materials. It should be quite trivial, for example, to use this method to produce 12-arm organic linkers for MOFs[44] or for covalent organic frameworks (COFs),[45] noting that 12-coordination is known for a number of theoretical net topologies,[46] but that this high level of coordination is difficult to access synthetically. Porous amorphous materials can also be prepared from these building blocks, such as the porous dendrimers described above. We also highlight that **RCC1**, or analogues, might offer an alternative to POSS-based materials for a variety of applications. Moreover, dodecafunctional POSS is isolated from polyphenylsilsesquioxane using a catalyst and is never the only product, necessitating separation.[38] By contrast, **RCC1** is easily prepared in good yields on a multigram scale in a one-pot process.

■ ASSOCIATED CONTENT

Supporting Information

Full synthetic and experimental details and gas sorption data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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