Supplementary Information for manuscript entitled:

Rapid Formation of Metal-Organic Nano-Capsules Gives New Insight Into the Self-Assembly Process

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Information comprises:

- Experimental details

- Crystallographic data

- Figures of the PgC_3OH Cu-MONC (Figures S1 and S2).

- Figures of the MALDI-TOF spectra collected for Cu-MONC's with PgC_2, PgC_4 – PgC_{11} and $Pg_{Isobutyl}$ (Figures S3 – S12).

- Description of the PgC_{12} and PgC_{13} bi-layer arrangements formed by crystallization from ethyl acetate (Figures S13 – S18).

Experimental

The *C*-alkylpyrogallol[4]arenes, except for PgC_{12} and PgC_{13} (see below) were synthesized by literature methods.[5b] Copper nitrate hemipentahydrate was purchased from Aldrich and used as supplied. General purpose grade solvents were used for the synthesis of Cu-MONC's, literature based Ga-MONC's (in the preparation of mixed metal MONC's),[7b] and hetero-Pg Cu-MONC's. As there is no way to determine the exact MW of the resulting Cu-MONC's or Cu/Ga-MONC's for all of the experiments,[S1] it was not possible to arrive at percentage yields for the precipitates formed. However, for each material formed, a mass of washed and dried precipitate has been listed. MALDI-TOF analysis (linear mode with dithranol as a matrix) has been used to identify all of the MONC's except the mixed metal case in which good X-ray diffraction data afforded a clear structural solution, albeit without clear identification of all metal ligands given the extensive disorder associated with the mixed metal sites.[S2] Given the expected broad nature of the mass spectrum, in addition to the fact that there is a small ΔM between Cu and Ga, MALDI-TOF analysis will most likely not help clarify the mixed metal situation. For this reason, ICP analysis was chosen as a characterizing technique. ICP analysis was performed by Galbraith Laboratories (Knoxville, TN, USA) on washed single crystals of the mixed metal MONC.

The paramagnetic nature of copper proved analysis of the PgC_3 Cu-MONC with ^{1}H NMR spectroscopy (in $CDCl_3$) to be troublesome, although it was possible to observe a number of broad peaks that suggested the presence of the pyrogallol[4]arene in the material.

Synthesis of PgC*n* Cu-MONC precipitates: In a general experiment, a known quantity of the desired *C*-alkylpyrogallol[4]arene was dissolved in the minimum amount of methanol. Addition of two hundred equivalents of methanolic copper(II) nitrate afforded, in each case, a fine brown precipitate that quickly settles to the bottom of the reaction vessel. For each Cu-MONC formed, the material was filtered on glass fiber filter paper, washed with methanol, and dried to afford a fine powder. Masses of powder obtained for each PgC*n* Cu-MONC obtained are outlined below, along with the starting amounts of each pyrogallol[4]arene used in MONC preparation.

PgC$_3$ Cu MONC: PgC$_3$ used = 1.05 g (1.46 mmol); Mass ppt formed = 0.94 g.

PgC$_2$ Cu MONC: PgC$_2$ used = 1.004 g (1.51 mmol); Mass ppt formed = 0.87 g.

PgC$_4$ Cu MONC: PgC$_4$ used = 1.02 g (1.31 mmol); Mass ppt formed = 0.96 g.

PgC$_5$ Cu MONC: PgC$_5$ used = 1.008 g (1.21 mmol); Mass ppt formed = 0.80 g.

PgC$_6$ Cu MONC: PgC$_6$ used = 1.001 g (1.13 mmol); Mass ppt formed = 1.03 g.

PgC$_7$ Cu MONC: PgC$_7$ used = 1.035 g (1.10 mmol); Mass ppt formed = 0.97 g.

PgC$_8$ Cu MONC: PgC$_8$ used = 1.026 g (1.03 mmol); Mass ppt formed = 0.85 g.

PgC$_9$ Cu MONC: PgC$_9$ used = 1.015 g (0.96 mmol); Mass ppt formed = 1.12 g.

PgC$_{10}$ Cu MONC: PgC$_{10}$ used = 1.01 g (0.91 mmol); Mass ppt formed = 0.81 g.

PgC$_{11}$ Cu MONC: PgC$_{11}$ used = 1.007 g (0.86 mmol); Mass ppt formed = 0.90 g.

PgC$_{isobutyl}$ Cu MONC: PgC$_{isobutyl}$ used = 1.002 g (1.29 mmol); Mass ppt formed = 0.88 g.

PgC$_{12}$ Cu MONC: PgC$_{12}$ used = 1.025 g (0.84 mmol); Mass ppt formed = 0.75 g.

PgC$_{13}$ Cu MONC: PgC$_{13}$ used = 1.014 g (0.79 mmol); Mass ppt formed = 0.83 g.

Modified Synthesis of tridecanal and tetradecanal: During the literature procedure for the synthesis of alkyl aldehydes,[S3] involving oxidation of the corresponding alcohol with pyridinium chlorochromate (PCC), the workup involves addition of Na_2SO_4 (and diethyl ether) to the reaction flask. This affords a black tar like material that is difficult to filter (and wash), and for this reason, experimentation with addition of Florisil, coupled with vigorous stirring afforded a flowing dark material that is easily filtered and washed, thus making workup easier. Note: stirring should not be stopped until Florisil addition is complete, otherwise vigorous working of the material with a spatula will be required, resulting in a less workable mixture.

Synthesis of PgC$_{12}$: Tridecanal (23.688 g, 0.119 mol) and pyrogallol (15.04 g, 0.119) were dissolved in ethanol (350 ml) and concentrated hydrochloric acid (15 ml) was added. The mixture was heated at reflux overnight and cooled to room temperature. Upon cooling, a white precipitate formed that was filtered, washed with cold ethanol (25 ml) diethyl ether (2 × 20 ml), and dried. The material was found to be an ethanol solvate of dodecylpyrogallol[4]arene, and the white powder was dried at 100 °C for two days under reduced pressure to afford the title compound with a trace of ethanol present (29.99 g, 82 %). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H: 8.779 (s, 1H, **OH/ArH**), 7.472 (s, 1H, **OH/ArH**), 6.888 (s, 1H, **OH/ArH**), 6.843 (s, 1H, **OH/ArH**), 4.380 (m, 1H, Ar**CH**Ar), 2.226 (m, 2H, ArCH**CH$_2$**), 1.256 (m, 20H, 10 × **CH$_2$**), 0.887 (t, 3H, CH$_2$**CH$_3$**, ^3J = 6 Hz). 13C NMR (300 MHz, CDCl$_3$) δ_C: 138.45, 137.30, 131.33, 125.34, 124.02, 113.74, 58.44, 34.06, 33.14, 31.91, 29.86, 29.76, 29.70, 29.37, 28.21, 22.66, 18.38, 14.07. MS: 2449.79 [2M-H]⁻, 1224.12 [M-H]⁻, 610.98 [M-2H]⁻.

Synthesis of PgC$_{13}$: Tetradecanal (14.75 g, 69.5 mmol) and pyrogallol (8.76 g, 69.5 mmol) were dissolved in ethanol (250 ml) and concentrated hydrochloric acid (9 ml) was added. The mixture was heated at reflux overnight and cooled to room temperature. Upon cooling, a white precipitate formed that was filtered, washed with cold ethanol (15 ml) diethyl ether (2 × 10 ml), and dried. The material was found to be an ethanol solvate of tridecylpyrogallol[4]arene, and the white powder was dried at 100 °C for two days under reduced pressure to afford the title compound with a trace of ethanol present (13.07 g, 59 %). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H: 8.784 (s, 1H, **OH/ArH**), 7.475 (s, 1H, **OH/ArH**), 6.891 (s, 1H, **OH/ArH**), 6.844 (s, 1H, **OH/ArH**), 4.382 (m, 1H, Ar**CH**Ar), 2.228 (m, 2H, ArCH**CH$_2$**), 1.277 (m, 22H, 11 × **CH$_2$**), 0.890 (t, 3H, CH$_2$**CH$_3$**, ^3J = 6 Hz). 13C NMR (300 MHz, CDCl$_3$) δ_C: 138.45, 137.30, 131.33, 125.34, 124.02, 113.76, 58.47, 34.07, 33.13, 31.91, 29.87, 29.75, 29.71, 29.68, 29.36, 28.23, 22.66, 18.34, 14.07. MS: 2561.41 [2M-H]$^-$, 1280.12 [M-H]$^-$, 639.14 [M-2H]$^-$.

Crystallization of PgC$_{12}$·EtOAc and PgC$_{13}$·EtOAc: In each case, 100 mg of the desired pyrogallol[4]arene was quantitatively re-crystallized from GPR grade ethyl acetate by slow evaporation. Upon nearing dryness, colorless single crystals that were suitable for X-ray diffraction experiments formed.

Synthesis / crystallization of mixed metal PgC$_3$ Cu/Ga MONC: Crystals of pre-formed PgC$_3$ Ga-MONC's were suspended in a mixture of acetone and methanol. A methanolic solution of copper(II) nitrate (200 equivalents) was added to suspension,

resulting in a color change from blue/green to red/brown in addition to instant dissolution of the suspended crystalline material. Slow evaporation of the solution overnight to a point nearing dryness resulted in the growth of red single crystals that are suitable for X-ray diffraction studies.

Synthesis of hetero-Pg (PgC$_6$ / PgC11) Cu–MONC's: In a general experiment similar to those for the homologous PgCn Cu-MONC's, an equimolar mixture of PgC$_6$ and PgC$_{11}$ was dissolved in a minimum amount of methanol. Addition of 200 equivalents of methanolic copper(II) nitrate to the solution resulted in the instant formation of a fine brown precipitate. This material was filtered, washed and dried prior to examination with MALDI-TOF mass spectrometry.

Crystallographic data

X-ray data were collected on a Bruker SMART 1000 CCD diffractometer. CCDC numbers 648029 - 648032 contain the crystallographic data files for the crystal structures reported in this manuscript. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: (international) +44 1223/336-033; Email: deposit@ccdc.cam.ac.uk].

Crystal data for partial structure of the PgC$_3$ Cu–MONC (CCDC 648029): C$_{120}$H$_{148.50}$Cu$_{12}$O$_{50.25}$, M = 3157.37, monoclinic, a = 36.361(5), b = 32.987(5), c = 24.640(4) Å, β = 92.526(4) °, U = 29526(7) Å^3, μ = 1.421 Mg/m^3, T = 173(2) K, space

group $C2/c$, $Z = 8$, Mo K$_\alpha$ radiation (wavelength $\lambda = 0.71073$ Å), GOF = 1.045, agreement index $R_1 = 0.2012$, 93490 reflections measured, 32600 unique ($R_{int} = 0.6463$) which were used in all calculations. The final $wR(F^2)$ was 0.4522 (all data). Given the quality of the data, many of the peaks around the MONC were modelled as disordered water molecules. The reported and calculated formulae differ due to the missing hydrogen atoms of waters of crystallization and the inability to assign the hydrogen atoms of the remaining 'upper rim' hydroxyl groups. The poor quality of the data meant that all atoms except for Cu were refined isotropically, and resulted in a lack of convergence during refinement. A number of the C-propyl chains of the pyrogallol[4]arenes were disordered over two positions and were modelled at partial occupancy.

Crystal data for the PgC$_{12}$·EtOAc bilayer arrangement (CCDC 648030):
C$_{81}$H$_{126}$O$_{16.75}$, $M = 1367.82$, triclinic, $a = 12.017(4)$, $b = 13.104(4)$, $c = 26.595(7)$ Å, $\alpha = 86.693(5)$, $\beta = 78.650(5)$, $\gamma = 77.855(5)°$, $U = 4013(2)$ Å^3, $\mu = 1.132$ Mg/m^3, $T = 173(2)$ K, space group $P\bar{1}$, $Z = 2$, Mo K$_\alpha$ radiation (wavelength $\lambda = 0.71073$ Å), GOF = 1.015, agreement index $R_1 = 0.0815$, 19667 reflections measured, 15765 unique ($R_{int} = 0.0233$) which were used in all calculations. The final $wR(F^2)$ was 0.2626 (all data).

Crystal data for the PgC$_{13}$·EtOAc bilayer arrangement (CCDC 648031):
C$_{91}$H$_{151.50}$O$_{18.75}$, $M = 1545.62$, triclinic, $a = 11.758(4)$, $b = 13.555(4)$, $c = 30.524(10)$ Å, $\alpha = 93.394(6)$, $\beta = 95.176(6)$, $\gamma = 108.457(5)°$, $U = 4576(3)$ Å^3, $\mu = 1.122$ Mg/m^3, $T = 173(2)$ K, space group $P\bar{1}$, $Z = 2$, Mo K$_\alpha$ radiation (wavelength $\lambda = 0.71073$ Å), GOF =

1.032, agreement index R_1 = 0.0846, 30900reflections measured, 19175 unique (R_{int} = 0.0439) which were used in all calculations. The final $wR(F^2)$ was 0.2619 (all data).

**Crystal data for the mixed metal PgC$_3$ Cu/Ga MONC (CCDC 648032):** $C_{122.75}H_{140.50}Cu_8Ga_4O_{45.50}$, M = 3131.05, triclinic, a = 21.206(3), b = 21.834(3), c = 23.544(5) Å, α = 110.972(2), β = 110.134(2), γ = 98.955(2)°, U = 9060(3) Å^3, μ = 1.148 Mg/m^3, T = 150(2) K, space group $P\bar{1}$, Z = 2, synchrotron radiation (wavelength λ = 0.69070 Å), GOF = 1.283, agreement index R_1 = 0.0816, 46495 reflections measured, 19010 unique (R_{int} = 0.0588) which were used in all calculations. The final $wR(F^2)$ was 0.2316(all data).

Figures of the PgC$_3$OH Cu-MONC.
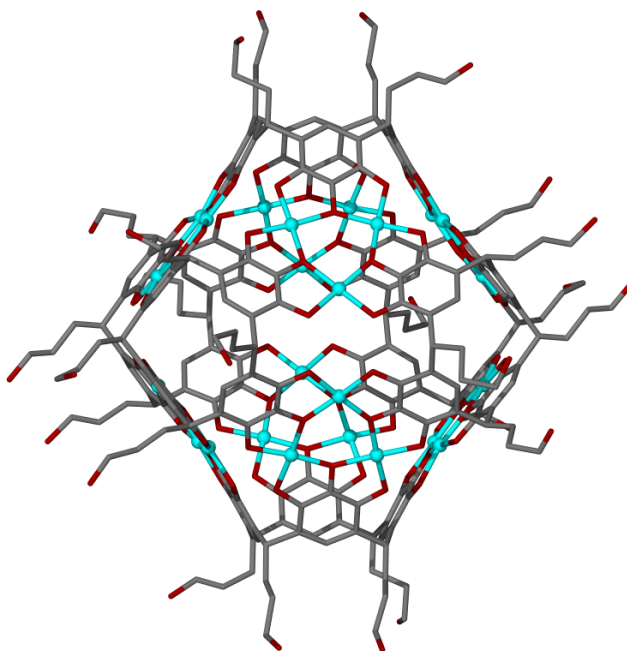
Figure S1. The Cu-MONC formed by reaction of PgC$_3$OH with Cu(II) (NO$_3$)$_2$ hemipentahydrate. Hydrogen atoms, solvents of crystallization and apical metal ligands removed for clarity.
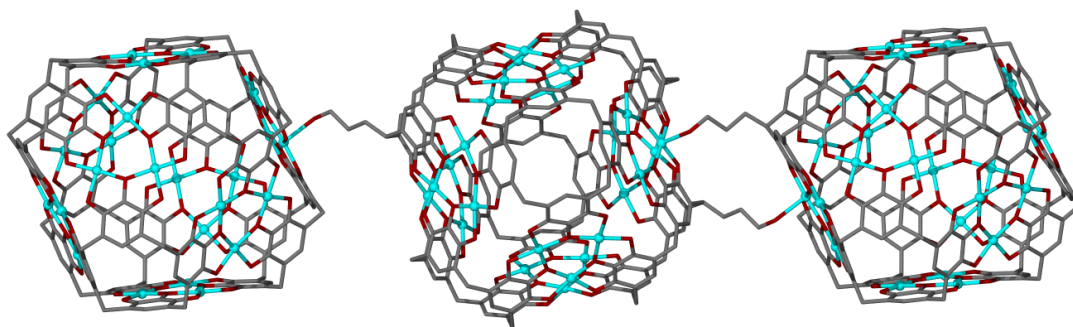
Figure S2. Part of the extended structure of the PgC$_3$OH Cu-MONC showing some of the coordination to Pg 'tails' to neighboring metal centers. Hydrogen atoms, solvents of crystallization and apical metal ligands removed for clarity.

Figures of the MALDI-TOF spectra collected for Cu-MONC's with PgC$_2$, PgC$_4$ – PgC$_{11}$ and Pg$_{Isobutyl}$.
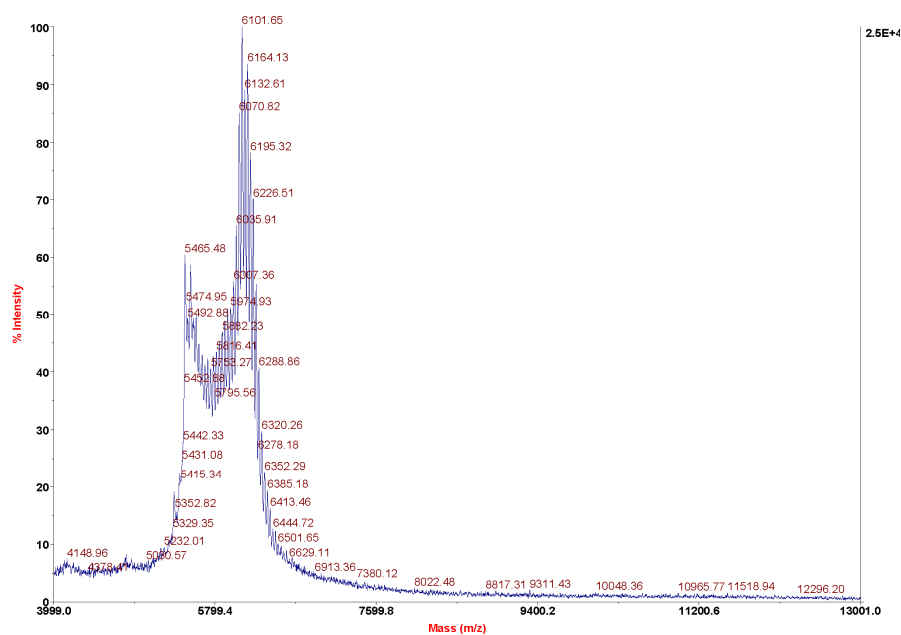
Figure S3. MALDI-TOF spectrum of the PgC$_2$ Cu-MONC.
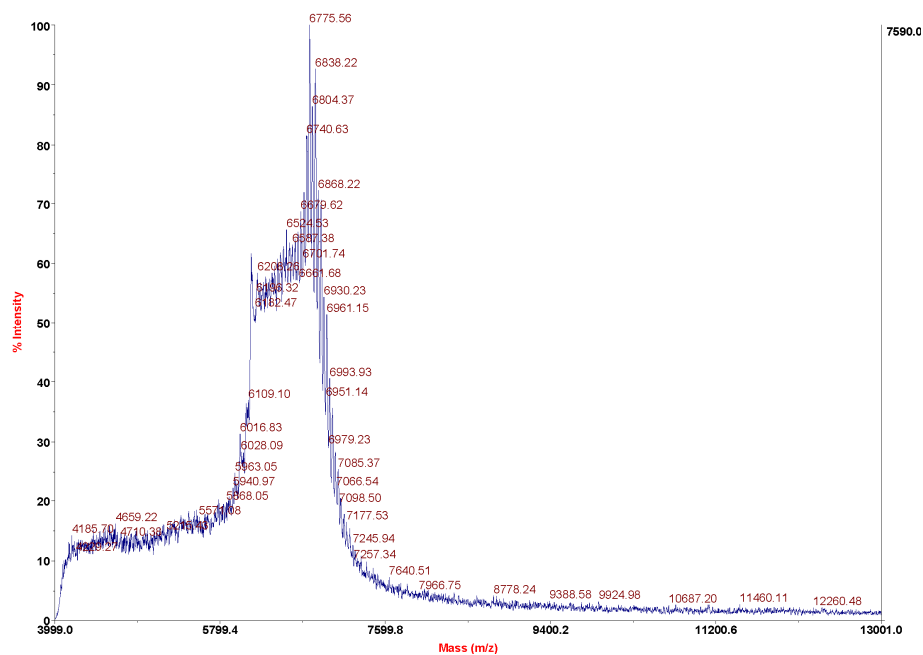
Figure S4. MALDI-TOF spectrum of the PgC$_4$ Cu-MONC.
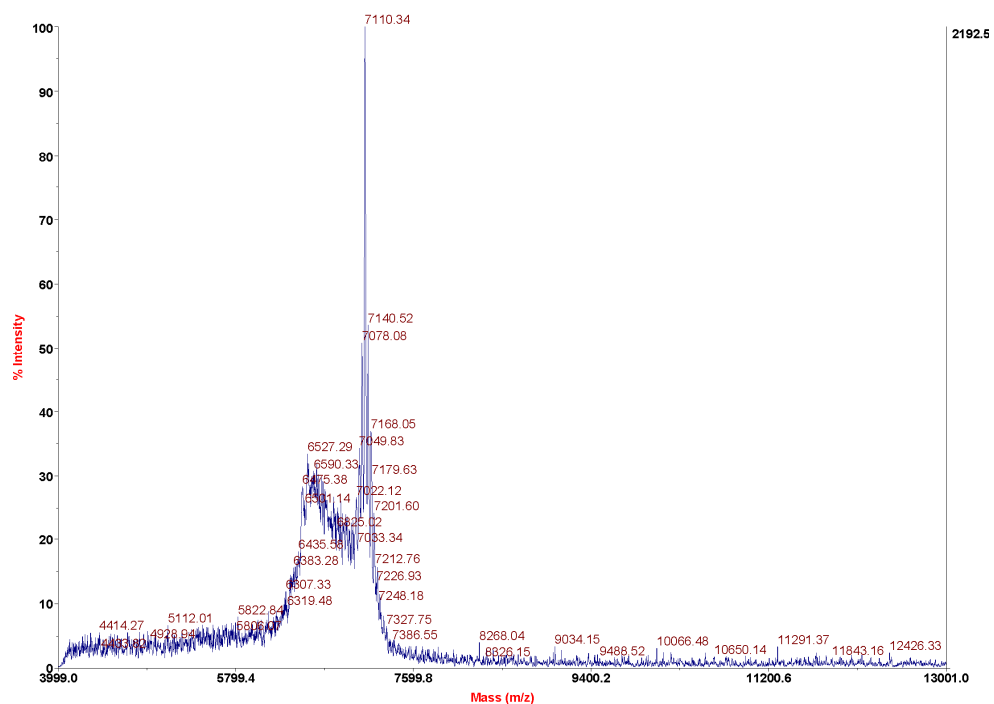
Figure S5. MALDI-TOF spectrum of the PgC$_5$ Cu-MONC.
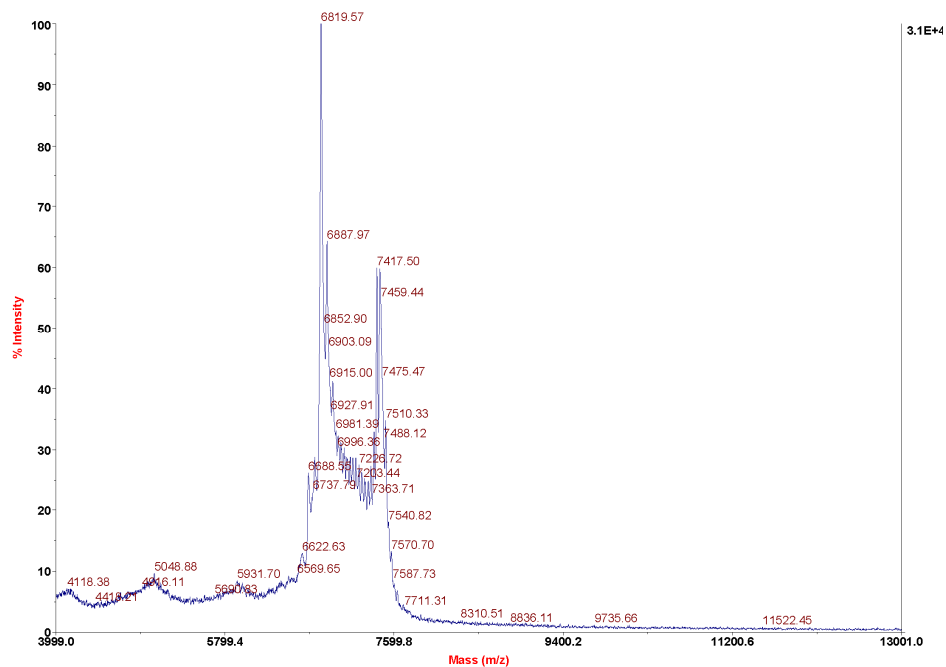
Figure S6. MALDI-TOF spectrum of the PgC$_6$ Cu-MONC.
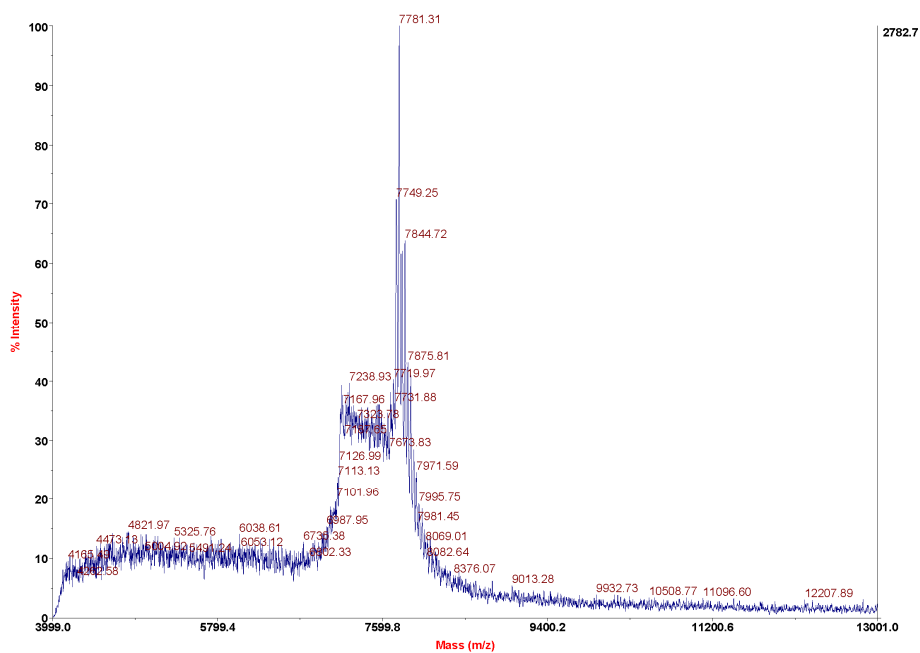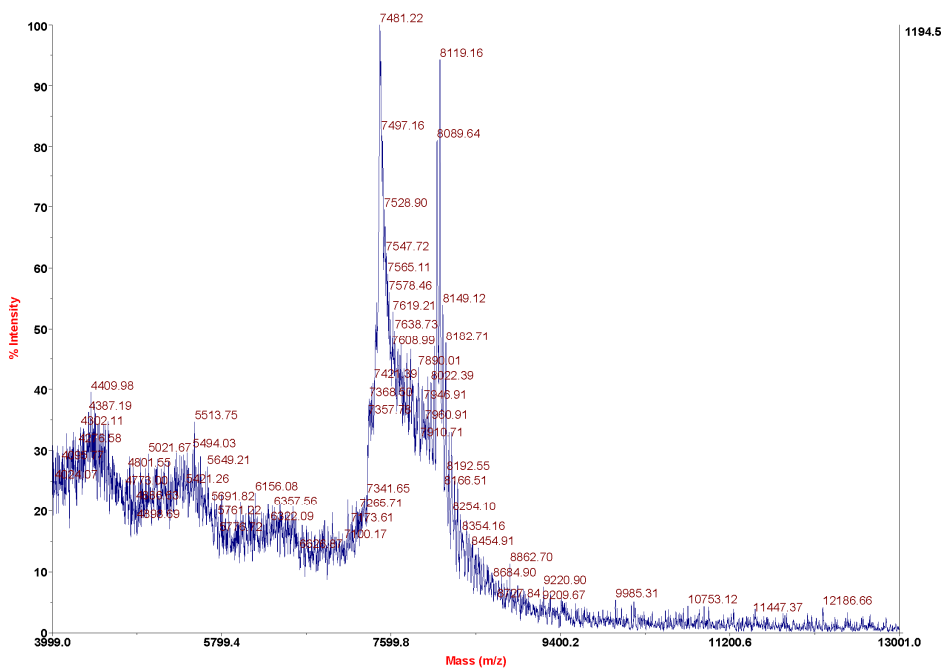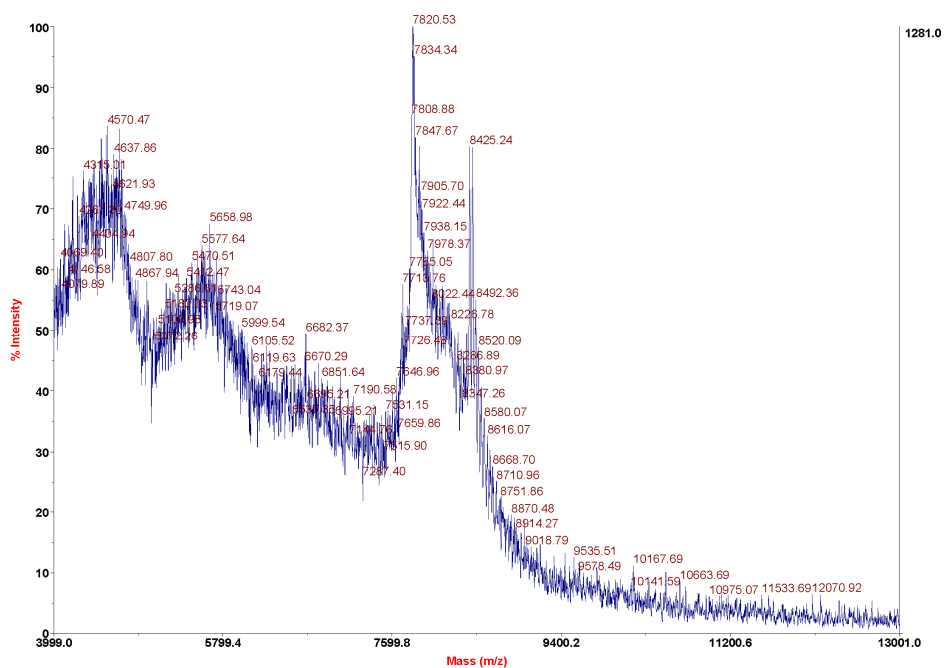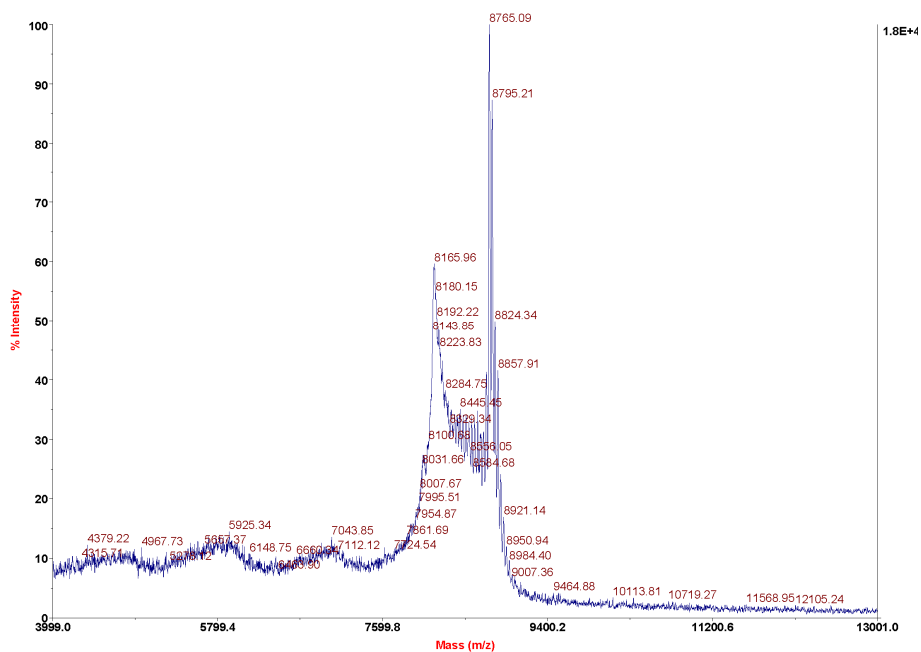
Figure S7. MALDI-TOF spectrum of the PgC$_7$ Cu-MONC.

Figure S8. MALDI-TOF spectrum of the PgC$_8$ Cu-MONC.

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Figure S9. MALDI-TOF spectrum of the PgC$_9$ Cu-MONC.
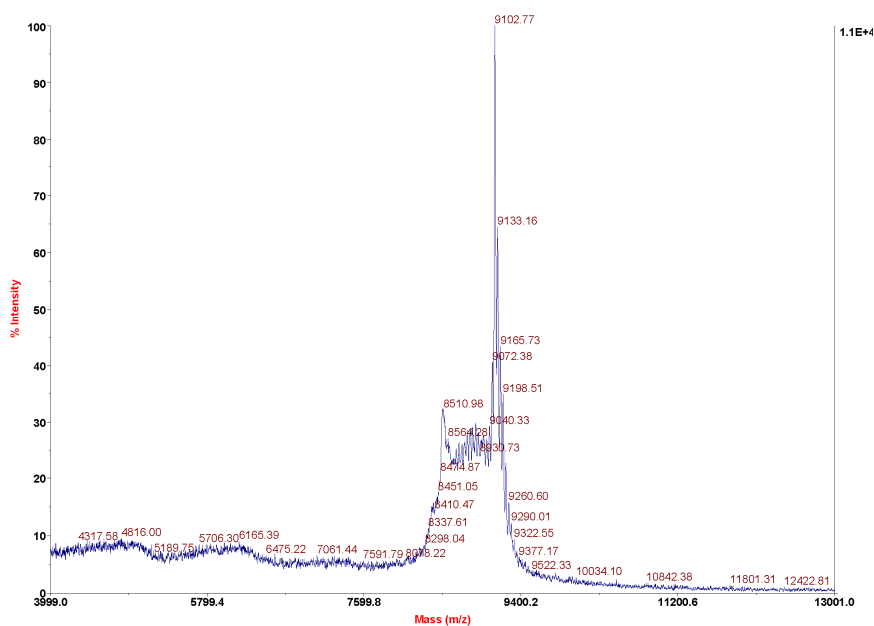

Figure S10. MALDI-TOF spectrum of the PgC$_{10}$ Cu-MONC.

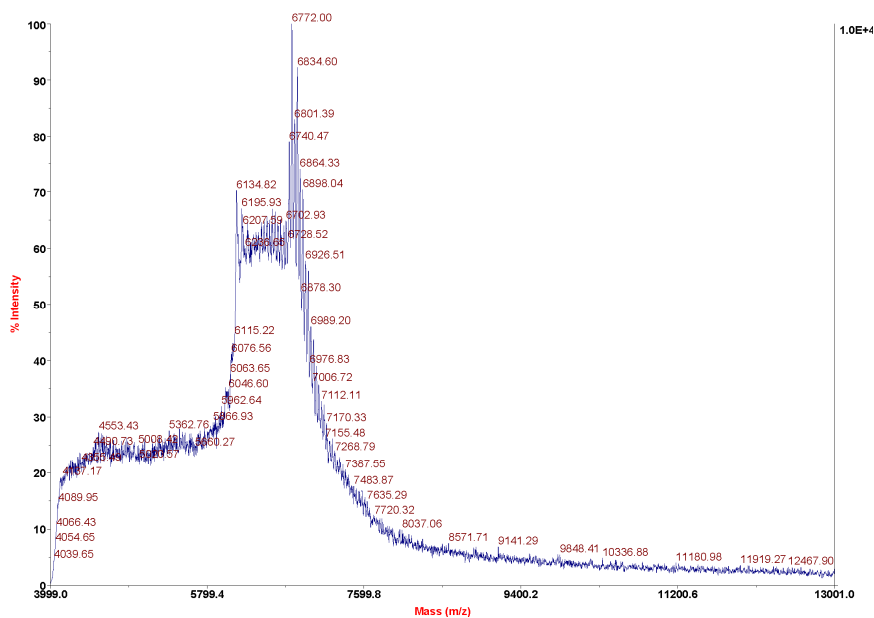**Figure S11.** MALDI-TOF spectrum of the PgC$_{11}$ Cu-MONC.


Figure S12. MALDI-TOF spectrum of the PgC$_{isobutyl}$ Cu-MONC.

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Description of the PgC$_{12}$ and PgC$_{13}$ bilayer arrangements formed when crystallized from ethyl acetate by slow evaporation.

The asymmetric unit of PgC$_{12}$·EtOAc contains one molecule of PgC$_{12}$, one and a half EtOAc molecules, and two waters of crystallization (Figure S13). It is presumed that the water molecules are present due to the GPR quality of the ethyl acetate in addition to slow evaporation in atmospheric conditions. Notably, such a water content is not found when 'sphere-forming' pyrogallol[4]arenes are crystallized from GPR EtOAc.
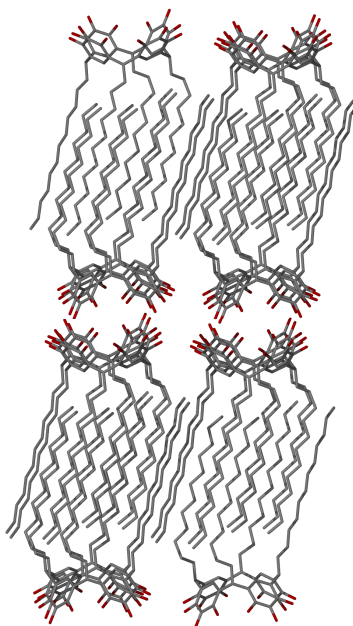
Symmetry expansion of the asymmetric unit shows the molecules to assemble in a slightly offset head-to-head arrangement around the disordered ethyl acetate molecule (shown only in one position in Figure S14). The extended structure also shows that the dodecyl chains of the cyclic tetramers interact through van der Waals interactions to form the extensive bi-layer similar to those reported and commented upon in the main body of the manuscript (Figure S15).
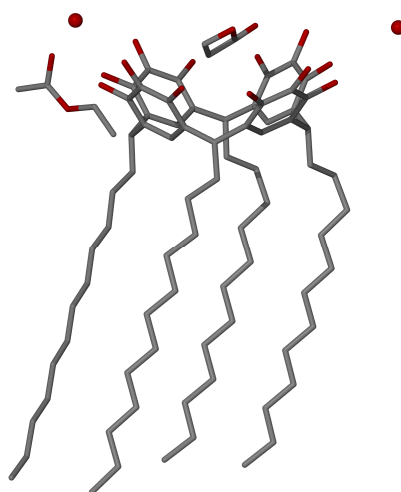
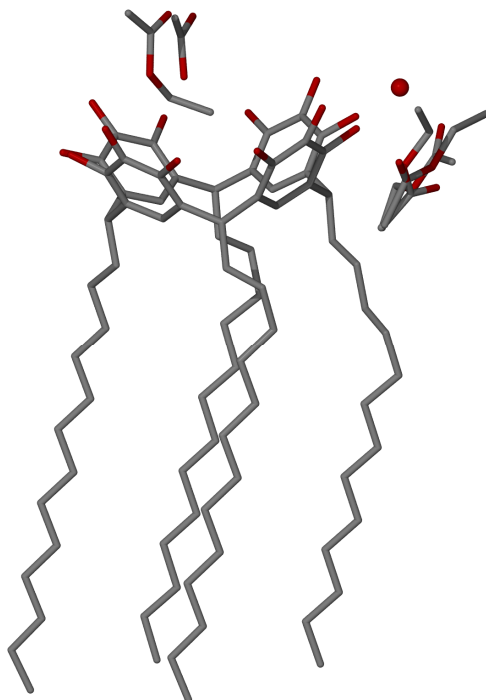**Figure S13.** The asymmetric unit in PgC$_{12}$ · EtOAc showing the disordered solvent in the cavity of the PgC$_{12}$.
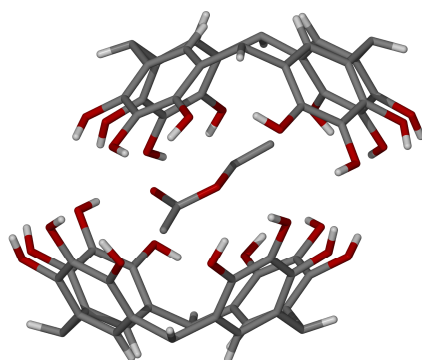
Figure S14. The offset dimeric capsule found in $PgC_{12} \cdot EtOAc$. The Pg lower rim alkyl chains, hydrogen atoms of the guest molecule, and other solvents of crystallization have been omitted for clarity. The disordered ethyl acetate molecule in the cavity of the capsule is only shown in one position for clarity.
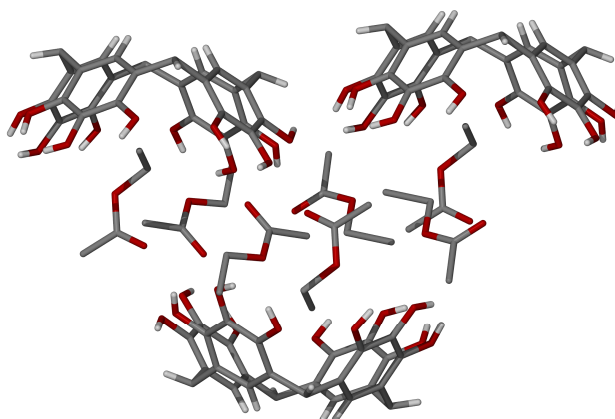

Figure S15. The extended structure in $PgC_{12} \cdot EtOAc$ showing the inter-digitation of the dodecyl chains. Hydrogen atoms, ethyl acetate and water molecules of crystallization are omitted for clarity.

The asymmetric unit of $PgC_{13} \cdot EtOAc$ contains one molecule of PgC_{13}, three ethyl acetates, and one and water of crystallization (Figure S16). As was the case for $PgC_{12} \cdot EtOAc$, it is presumed that the water molecules are present due to the GPR quality of the ethyl acetate in addition to slow evaporation in atmospheric conditions. Symmetry expansion of the asymmetric unit shows the molecules to assemble in a markedly different fashion to those in $PgC_{12} \cdot EtOAc$. The molecules are completely offset in the present structure and there are numerous ethyl acetate molecules sandwiched in the hydrogen-bonding layer (shown to some extent in Figure S17). The extended structure also shows that the tridecyl chains of the cyclic tetramers interact through van der Waals interactions to form the extensive bi-layer similar to the example for $PgC_{12} \cdot EtOAc$, and those reported and commented upon in the main body of the manuscript (Figure S18).

Figure S16. The asymmetric unit in $PgC_{13} \cdot EtOAc$.

Figure S17. The offset bi-layer arrangement found in PgC$_{13}$ · EtOAc showing the large number of ethyl acetate molecules found between the 'heads' of the pyrogallol[4]arenes. The Pg lower rim alkyl chains, hydrogen atoms of the ethyl acetates, as well as waters of crystallization have been omitted for clarity.
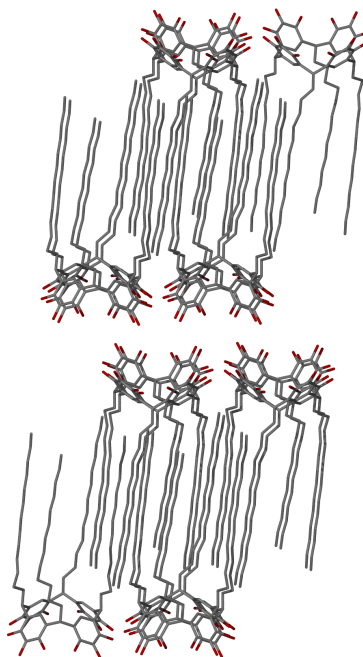
Figure S18. The extended structure in PgC$_{13}$ · EtOAc showing the inter-digitation of the tridecyl chains. Hydrogen atoms, ethyl acetate and water molecules of crystallization are omitted for clarity.

References

[S1] Although the dilution of the PgC$_n$Cu-MONC:matrix was found to play some role in the intensity of the shoulder peak, we cannot accurately determine an average molecular weight (MW) to calculate accurate MALDI-TOF concentrations. The fact that the shoulder is *always* present is indicative that there are numerous capsule solvent occupancies that would invariably preclude the possibility of an average MW calculation.

[S2] The poorly diffracting nature of the crystals may be attributable to partially occupied coordination spheres of the copper centers, as well as the interior of the resulting capsules, features that would cause extreme disorder when averaged through a crystal.

[S3] A. Naoki, F. Nobuhiro, M. Shigeki, *J. Nat. Prod.*, 2001, **64**, 1210.