



Heriot-Watt University  
Research Gateway

## Investigations into the assembly behaviour of a 'rigidified' p-carboxylatocalix[4]arene

### Citation for published version:

Fairbairn, RE, Teat, SJ, Ling, I & Dalgarno, SJ 2019, 'Investigations into the assembly behaviour of a 'rigidified' p-carboxylatocalix[4]arene', *CrystEngComm*, vol. 21, no. 43, pp. 6659-6665.  
<https://doi.org/10.1039/C9CE01326A>

### Digital Object Identifier (DOI):

[10.1039/C9CE01326A](https://doi.org/10.1039/C9CE01326A)

### Link:

[Link to publication record in Heriot-Watt Research Portal](#)

### Document Version:

Peer reviewed version

### Published In:

CrystEngComm

### Publisher Rights Statement:

This document is the Accepted Manuscript version of a Published Work that appeared in final form in CrystEngComm. The final authenticated version is available online at: <http://dx.doi.org/10.1039/C9CE01326A>

### General rights

Copyright for the publications made accessible via Heriot-Watt Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

### Take down policy

Heriot-Watt University has made every reasonable effort to ensure that the content in Heriot-Watt Research Portal complies with UK legislation. If you believe that the public display of this file breaches copyright please contact [open.access@hw.ac.uk](mailto:open.access@hw.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.

# Investigations into the assembly behaviour of a 'rigidified' *p*-carboxylatocalix[4]arene

Robyn E. Fairbairn,<sup>a</sup> Simon J. Teat,<sup>b</sup> Irene Ling<sup>\*c</sup> and Scott J. Dalgarno<sup>\*a</sup>

Received 00th January 20xx,  
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

d

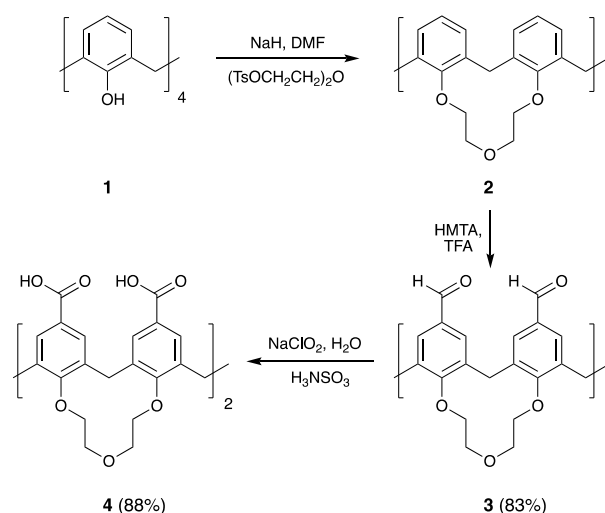
The *p*-carboxylatocalix[4]arenes have been shown to be versatile supramolecular building blocks capable of forming a range of bi-layers, capsules and nanoscale tubules in the solid state. Here we report the synthesis of a new 'rigidified' analogue, as well as investigations into its self-assembly and related coordination chemistry. These behaviours are reminiscent of other *p*-carboxylatocalix[4]arenes despite the presence of rigidifying groups at the lower-rim, suggesting that this building block may be further exploited in the assembly of a range of new metal-organic cages and coordination polymers.

## Introduction

Calix[*n*]arenes are cyclic polyphenols that have found widespread use in the development of the field of supramolecular chemistry.<sup>1-4</sup> This is in part due to their possessing hydrophobic cavities capable of playing host to a variety of different types of guest,<sup>5</sup> but also because they can be synthetically modified at either the upper- or lower-rim (or both) to afford an enormous range of versatile building blocks.<sup>6</sup> Calix[4]arene (C[4], **1**, Scheme 1) and its many synthetic derivatives have been widely employed in crystal engineering studies as they have well understood conformational properties that can be controlled through synthesis,<sup>7,8</sup> and other tuneable features such as solubility in aqueous media (e.g. *p*-sulfonatocalix[4]arene).<sup>6</sup> With respect to conformational versatility, it is possible to lock the C[4] framework in cone, partial cone, 1,2-alternate, and 1,3-alternate conformations through lower-rim etherification.<sup>8,9</sup> This can be achieved in relatively good yields in most cases *via* the use of a suitable base that is able to act as a template, and an alkylating agent of suitable length (typically propyl or longer) and bulk to prevent interconversion through the C[4] annulus.

The *p*-carboxylatocalix[*n*]arenes (*p*CO<sub>2</sub>[*n*]s) are a family of building blocks that have received relatively little attention to date. This is surprising given their potential to form fascinating structures through varied supramolecular synthons or coordination chemistry templates.<sup>10,11</sup> We have studied a series of *p*CO<sub>2</sub>[4]s, predominantly in the cone conformation, and our first investigation focused on the use of pyridine as a guest

template for the assembly of *p*-carboxylatocalix[4]arene.<sup>12</sup> In that case the components formed dimeric hydrogen-bonded capsules through the common Py...CO<sub>2</sub>H heterosynthon,<sup>13</sup> and the calixarenes were found to pack in a parallel back-to-back manner, forming infinite nanotubes as a result (Figure 1A). Subsequent studies with a range of *p*CO<sub>2</sub>[4]s and pyridine based guest templates formed various anti-parallel bi-layer structures,<sup>14</sup> except in the case of the lower-rim di-propoxy *p*CO<sub>2</sub>[4]s in which the upper-rim was either tris- or tetra-functionalised with carboxyl groups.<sup>15-17</sup> In those particular cases the calixarenes have a tendency to form triply helical nanotubes akin to the parent building block,<sup>18</sup> and crystallisation of these *p*CO<sub>2</sub>[4]s from pyridine allowed for modulation of the inter-tubule spacing, again through formation of dimeric hydrogen-bonded capsules (Figure 1B).<sup>15</sup>



**Scheme 1.** Synthetic route to *p*-carboxylatocalix[4]arene bis-crown-3 (**4**) *via* formylation of calix[4]arene bis-crown-3 and subsequent oxidation.

<sup>a</sup> Institute of Chemical Sciences, William Perkin Building, Heriot-Watt University, Riccarton, Edinburgh, Scotland EH14 4AS, UK. Email: [S.J.Dalgarno@hw.ac.uk](mailto:S.J.Dalgarno@hw.ac.uk)

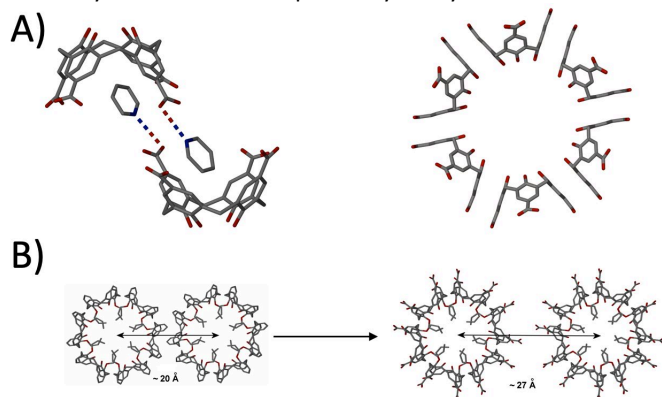
<sup>b</sup> Lawrence Berkeley National Laboratory, 1 Cyclotron Road, MS 6R2100, Berkeley, California 94720, USA.

<sup>c</sup> School of Science, Monash University Malaysia, Jalan Lagoan Selatan, Bandar Sunway, 46150 Selangor, Malaysia. E-mail: [ireneling@monash.edu](mailto:ireneling@monash.edu)

Electronic Supplementary Information (ESI) available: Crystallographic Information Files (CIFs). See DOI: 10.1039/x0xx00000x

We have also investigated metal-directed assembly of a number of these molecules and have reported the formation of a range of coordination polymers<sup>19</sup> and discrete metal-organic

cages<sup>11,20</sup> that host a variety of solvent molecules (either ligated or freely occupying the  $p\text{CO}_2[4]$  cavities). It is worth noting that de Mendoza and co-workers reported the formation of spectacular giant polyhedra comprising tetra-propoxy  $p\text{CO}_2[4]$  or  $p\text{CO}_2[5]$  (octahedral or icosahedral cages, respectively), the assembly of which was templated by uranyl ions.<sup>21</sup>



**Figure 1.** A) Hydrogen-bonded head-to-head dimer formed by crystallisation of  $p\text{CO}_2[4]$  from pyridine, and extended structure showing nanotube formation.<sup>12</sup> B) Modulation of nanotube packing by introduction of carboxyl groups to the upper-rim of di-propoxy calix[4]arene.<sup>15</sup>

In the present contribution we report our first investigations into the self- and metal-directed assembly of a 'rigidified'  $p\text{CO}_2[4]$ , with conformational restriction having been achieved through lower-rim bis-crown ether formation. This new host adopts a pseudo- $C_4$  cone conformation and is thus ideal for comparison with the behaviours of  $p\text{CO}_2[4]$ s studied previously. We have attempted crystallisation of this new molecule from a range of pyridine guests, induced salt formation using 2-aminopyridine (2-AP) simultaneously as a guest template, and have also undertaken preliminary coordination chemistry studies with this building block in the presence of pyridine as a ligand / solvent. Single crystals were obtained in a number of cases, and the results suggest that this rigidified  $p\text{CO}_2[4]$  may be an excellent candidate for combination with structurally directing units to afford diverse metal-organic cages and 2-/3-D coordination polymers in future studies.

## Results and Discussion

Calix[4]arene-crown ethers (or calix[4]crowns) are C[4]s with polyether chains on the lower-rim that act as bridges between two aryl units within the macrocyclic framework. They have been shown to exhibit an affinity for alkali metal ions, the propensity for which relates to size of the crown ether loop at the lower-rim.<sup>7-8,22-23</sup> There are two general groups into which the calix[4]crowns can be separated, mono-crowns and bis-crowns. Lower-rim bridging in the former can either be between the 1,3-<sup>24</sup> or 1,2-positions,<sup>25-26</sup> known as distal and vicinal respectively, and the 1,3-bridged calix[4]crowns have generally attracted greater attention thanks to the more challenging synthesis associated with their 1,2- analogues. Bis-crowns can also bridge in different ways depending on the particular C[4] conformation, these being 1,3;2,4 or 1,2;3,4 for 1,3-alternate and cone conformers respectively. Compound **2** belongs to the

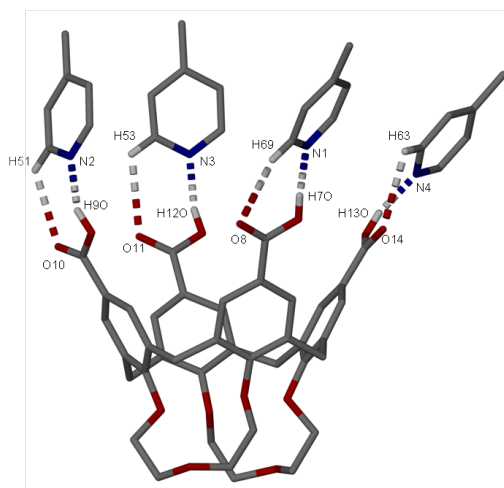
latter category and was synthesised according to literature procedure<sup>28</sup> by reaction of **1** diethylene glycol ditosylate in the presence of excess NaH.<sup>5</sup>

As stated above, restricting the compound with these relatively rigid chains prevents conformational interconversion and leaves the upper-rim amenable to further functionalisation. Compound **2** was reacted with TFA and an excess of HMTA over a 24 hour period<sup>29</sup> to produce the tetraformyl-calix[4]arene bis-crown-3 (**3**, Scheme 1). <sup>1</sup>H NMR analysis of an initial attempt at this synthesis revealed the presence of the target compound and a small amount of the *tris*-formylated biscrown-C[4] in the crude. Column chromatography was therefore carried out to separate these two products and it was found that the yield of the *tris*-formylated product was minimal in comparison to that of compound **3**. Subsequent reactions were carried out for longer periods at reflux and were found to give full conversion to compound **3**. Although this is the case, it is worth noting that shorter reaction times offer a relatively convenient route to *tris*-functionalised biscrown-C[4]. A subsequent Pinnick-type oxidation in water with sodium chlorite and sulfamic acid afforded compound **4** in good yield (Scheme 1).<sup>30</sup>

As outlined above, we previously studied the use of pyridine-based guest templates in the self-assembly of  $p\text{CO}_2[4]$ s with a view to understanding their self-assembly properties.<sup>12,14-17</sup> With compound **4** in hand, we first explored its ability to self-assemble in the presence of pyridine-based guest templates. In line with previous work, crystallisation of **4** was attempted from pyridine (Py), 2-picoline (2-Pic), 3-picoline (3-Pic) and 4-picoline (4-Pic) acting as both solvent and potential template.<sup>†</sup> Crystallisation was also attempted from other common solvents, but single crystals suitable for diffraction studies were only obtained in the case of 4-Pic.

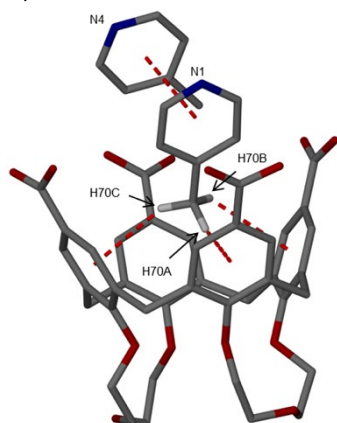
### Single crystal X-ray structure of *p*-carboxylatocalix[4]arene-bis-crown-3-4-picoline, **5**

Crystals of *p*-carboxylatocalix[4]arene-biscrown-3-4-Pic (**5**) were obtained upon slow evaporation of the solvent over a period of several days. The small colourless blocks were not suitable for study using an in-house diffractometer as it was only possible to obtain a partial structure solution, but publication quality data were subsequently obtained using synchrotron radiation. Single crystals of **5** were found to be in an orthorhombic cell and the structure solution was performed in the space group  $Pna2_1$ . The asymmetric unit (ASU) consists of one molecule of **4** and four molecules of 4-Pic (Figure 2). Inspection of Figure 2 shows that compound **4** adopts the cone conformation as expected due to the presence of the rigidifying ether chains at the lower-rim. As has been observed in previous studies of the pyridine templated assembly of various  $p\text{CO}_2[4]$ s, all four 4-Pic molecules in the ASU interact with the upper-rim  $\text{CO}_2\text{H}$  groups via formation of the common  $\text{Py}\cdots\text{CO}_2\text{H}$  heterosynthon. This occurs in this case with four symmetry unique  $\text{N}\cdots\text{HOCO}$  interactions with distances ranging from 1.736 – 1.852 Å, and four  $\text{CH}\cdots\text{OCOH}$  interactions with distances ranging from 2.606 – 2.720 Å.



**Figure 2.** Single crystal X-ray structure of the asymmetric unit in **5**. Hydrogen bonding interactions are shown as split-colour dashed lines. Hydrogen atoms (apart from those involved in the hydrogen bonding interactions) are omitted for clarity. Selected atoms have been labelled according to discussion.

Symmetry expansion of the ASU in **5** reveals that the cavity of **4** is occupied by a symmetry equivalent (s.e.) 4-Pic, leading to two 4-Pic molecules interacting with one another *via* a  $\pi$ -stacking interaction as shown in Figure 3; this occurs with an aromatic centroid...aromatic centroid distance of 3.564 Å. This also reveals the presence of three CH... $\pi$  interactions located between the hydrogen atoms on the methyl group of the 4-Pic molecule and the aromatic ring with a H[70A]...aromatic centroid distance of 2.609 Å, a H[70B]...aromatic centroid distance of 3.077 Å and a H[70C]...aromatic centroid distance of 2.938 Å (Figure 3).



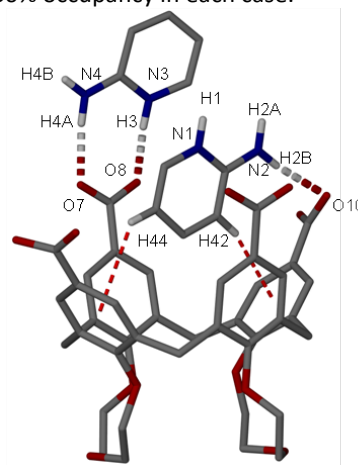
**Figure 3.** Symmetry expansion around **4** in the structure of **5** showing CH... $\pi$  and  $\pi$ ... $\pi$  interactions as red dashed lines. Hydrogen atoms (apart from those involved in CH... $\pi$  interactions) have been omitted for clarity. Selected atoms have been labelled according to discussion.

Following the study based on crystallisation from pyridine-based solvents, we then explored the effect of salt formation *via* the use of 2-aminopyridine (2-AP) as a **guest template**. In previous work,<sup>10</sup> reaction of lower-rim di-propoxy pCO<sub>2</sub>[4]s with 2-AP resulted in the formation of dimeric head-to-head capsules through salt formation and complementary self-assembly. In addition, even tetra-alkoxy pCO<sub>2</sub>[4]s behaved similarly despite their typically adopting pinched cone conformations in the solid state. This was presumed to be due

to deprotonation of the carboxyl groups by the 2-AP, resulting in charge repulsion at the proximal groups in the pinched cone and opening of the cavity for occupation by the cationic guest. **Reaction of 4** with 2-AP produced analogous salt formation as outlined below, with dimeric head-to-head capsule formation occurring as a result.

#### Single crystal X-ray structure of [(4-4H)(2-AP+H)<sub>4</sub>].(H<sub>2</sub>O)<sub>4</sub>, **6**

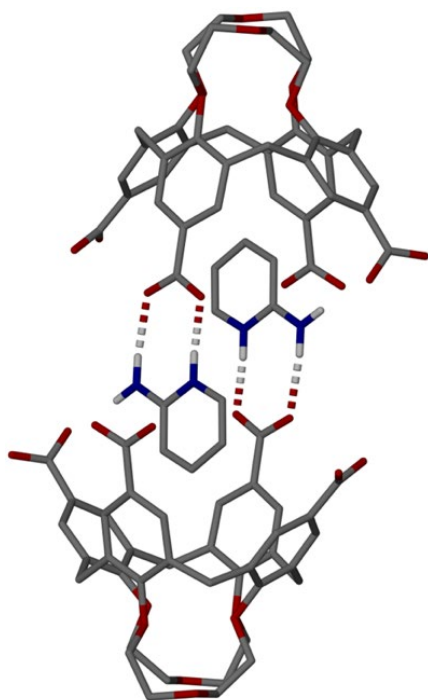
Single crystals of the salt [(4-4H)(2-AP+H)<sub>4</sub>].(H<sub>2</sub>O)<sub>4</sub>, **6**, were obtained as the result of the addition of compound **4** to 3 mL of MeOH. The resulting suspension was heated and 2-AP was added slowly until the suspension became a clear solution. Colourless plate-shaped crystals that were suitable for X-ray diffraction studies formed overnight. Crystals of the salt **6** were found to be in a monoclinic cell and structure solution was performed in the space group *P*2<sub>1</sub>/*n*. The ASU consists of one tetra-anion of **4** (4-4H, upper-rim CO<sub>2</sub>H groups deprotonated), four 2-aminopyridinium cations and four waters of crystallisation (Figure 4). Three of the water molecules present in the ASU are disordered over two positions and were modelled at 50% occupancy in each case.



**Figure 4.** Part of the asymmetric unit found in the X-ray crystal structure of salt **6**. Hydrogen bonding and CH... $\pi$  interactions are shown as split-colour and red dashed lines respectively. Hydrogen atoms (apart from those involved in hydrogen bonding and CH... $\pi$  interactions) have been omitted for clarity. Selected atoms have been labelled according to discussion.

Inspection of Figure 4 shows that the cavity of (4-4H) is occupied by one (2-AP+H) cation and that there are two CH... $\pi$  interactions between the guest *meta* hydrogen atoms and the aromatic rings of the host. The two symmetry unique CH...aromatic centroid distances associated with this (2-AP+H) cation guest molecule are observed with H[42]...aromatic centroid and H[44]...aromatic centroid distances of 2.731 and 3.240 Å, respectively. In addition, there is an HNH...OCO hydrogen bonding interaction between the cation guest and an upper-rim CO<sub>2</sub><sup>-</sup> group on the calixarene host. This symmetry unique HNH...OCO hydrogen bonding interaction has an H[2B]...O[10] distance of 2.193 Å. Symmetry expansion around the cationic guest in **6** results in formation of a hydrogen-bonded head-to-head dimer facilitated by both HNH...OCO and NH...OCO hydrogen bonding interactions (Figure 5), all of which mimics behaviour observed in previous work on salt formation

with  $p\text{CO}_2[4]s$ .<sup>10</sup> Within the head-to-head dimer there is one  $\text{NH}\cdots\text{OCO}$  and one  $\text{HNH}\cdots\text{OCO}$  hydrogen bonding interaction with respective  $\text{H}[1]\cdots\text{O}[11]$  and  $\text{H}[2\text{A}]\cdots\text{O}[12]$  distances of 1.782 and 2.011 Å. The three remaining (2-AP+H) cations interact with the remaining upper-rim  $\text{CO}_2^-$  groups *via* three  $\text{HNH}\cdots\text{OCO}$  hydrogen bonding interactions (distances ranging from 1.905 – 2.009 Å) and three  $\text{NH}\cdots\text{OCO}$  hydrogen bonding interactions (distances ranging from 1.762 – 1.779 Å). Further symmetry expansion shows that the dimers are arranged in the common anti-parallel bi-layer arrangement often observed for C[4]s, despite the presence of the lower-rim ether linkers being present (which one might expect to disrupt this favourable arrangement).



**Figure 5.** The hydrogen-bonded head-to-head dimer found in the extended crystal structure of **6**. Hydrogen bonding interactions are shown as split-colour dashed lines. Hydrogen atoms (apart from those involved in the hydrogen bonding interactions) are omitted for clarity.

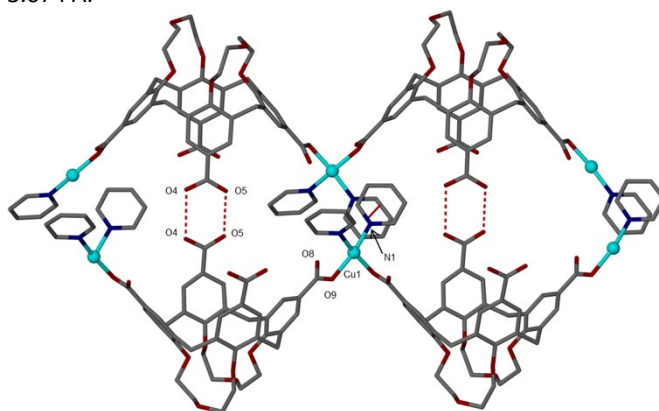
Having observed typical behaviours in the self-assembly of **4** above, the final aspect to this investigation was to explore coordination chemistry in the presence of selected transition metal ions when using pyridine as a solvent. This is an approach that we have employed previously considering the excellent solubility of  $p\text{CO}_2[4]s$  in pyridine, but also because benzoates have often been found to form polynuclear clusters under such conditions, the result of which could be interesting from a structure directing perspective, or from the perspective of imparting structural stability in the prevailing assembly / coordination polymer. In this regard, transition metal ions such as Ni(II), Mn(II), Cu(II) and Co(II) are known to form binuclear aqua-bridged complexes in the presence of benzoic acids and *N*-donor ligands in the presence of methanol, and have been investigated as potential directing centres, subsequently enabling control over  $p\text{-CO}_2[4]$  assembly.<sup>31</sup>

Compound **4** was added to methanolic solutions of either Ni(II), Mn(II), Cu(II) and Co(II) nitrate in a combinatorial manner,

affording a suspension in each case. Dropwise addition of pyridine was undertaken with gentle heating until dissolution was observed and the solutions were left to crystallise. Single crystals were obtained in three cases, two of which were found to be isostructural.

#### Single crystal X-ray structure of $[\text{Cu}^{\text{II}}\text{PyC}(4\text{-}2\text{H})(\text{Py})_2]$ , **7**

Crystals of the coordination polymer  $[\text{Cu}^{\text{II}}\text{PyC}(47\text{-}2\text{H})(\text{Py})_2]$ , **7**, were formed by the method outlined above with slow evaporation taking place over several weeks. The resulting small green/blue blocks were suitable for diffraction studies using synchrotron radiation only, as they were found to be weakly diffracting with a laboratory source. Crystals of **7** were found to be in an orthorhombic cell and structure solution was performed in the space group  $C222_1$ . The ASU consists of one half of the di-anion of **4** coordinated in a chelate manner to a distorted octahedral Cu centre (Cu[1]-O[9] and a long interaction Cu[1]-O[8] with bond distances of 1.970(3) Å and 2.570(4) Å) that is also coordinated to one crystallographically unique Py (Cu[1]-N[1] distance of 1.978(5) Å). Symmetry expansion reveals the formation of a 1-D coordination polymer as shown in Figure 6. These interwoven pairs of 1-D chains assemble to form bi-layer type arrays frequently observed for C[4] building blocks.<sup>32</sup> One of the  $\text{CO}_2\text{H}$  groups is disordered over two positions and was modelled at 50% occupancy in each. There was also diffuse electron density associated with a molecule of pyridine residing in each calixarene cavity, but disordered over three positions. Additional diffuse density associated with other solvent of crystallisation could not be modelled appropriately so the routine SQUEEZE was applied to the data.<sup>33</sup> This had the effect of dramatically improving the agreement indices during refinement for **7**. Symmetry expansion of **7** reveals the presence of a  $\pi$ -stacking interaction present between two pyridine molecules that are ligated to the Cu metal centre, occurring with an aromatic centroid $\cdots$ aromatic centroid distance of 3.506 Å. Hydrogen atoms were not placed on the upper-rim  $\text{CO}_2\text{H}$  groups due to disorder but homosynthon hydrogen bonding occurs in the off-set head-to-head arrangement with O $\cdots$ O distances ranging from 2.626 – 3.074 Å.



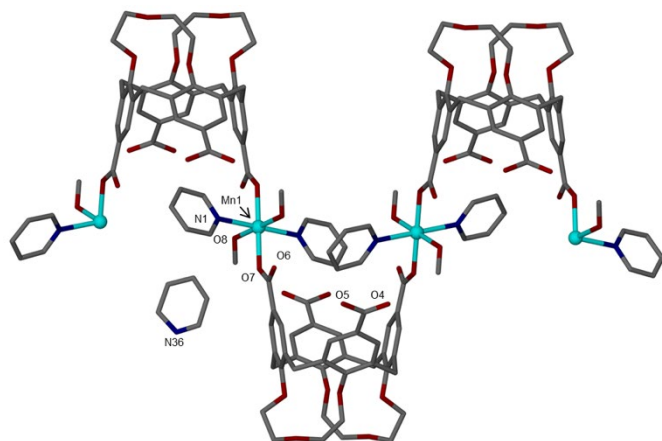
**Figure 6.** Partial extended structure of **7** showing interwoven 1-D coordination polymer chains. Hydrogen bonding between carboxyl groups and  $\pi$ -stacking interactions are shown as red dashed lines. Selected atoms have been labelled according to discussion. The disordered upper-rim  $\text{CO}_2\text{H}$  group is shown in one of two disordered positions.



Hydrogen atoms and the disordered Py occupying each calixarene cavity have been omitted for clarity.

### Single crystal X-ray structure of $[\text{Mn}^{\text{II}}(4\text{-2H})(\text{Py})_2(\text{MeOH})]\cdot\text{Py}(\text{H}_2\text{O})_2$ , **8**

Crystals of the coordination polymer  $[\text{Mn}^{\text{II}}(4\text{-2H})(\text{Py})_2(\text{MeOH})]\cdot\text{Py}(\text{H}_2\text{O})_2$ , **8**, were also formed by the method outlined above with slow evaporation taking place over several weeks. The small orange blocks were also weakly diffracting so were examined using synchrotron radiation. Crystals of **8** were found to be in a monoclinic cell and structure solution was performed in the space group  $C2/c$ . The ASU consists of one half of a di-anionic **4** coordinated to one octahedral Mn centre, which also has one ligated Py and a ligated methanol that was found to be disordered (modelled at 50% occupancy). The ASU also contains a disordered pyridine molecule (modelled at 50% occupancy) and two water molecules, one of which is disordered over two positions and modelled at 50% accordingly in each. Symmetry expansion reveals the formation of a coordination polymer as shown in Figure 7. In a similar way to that observed in complex **7**, the 1-D chains in **8** assemble to build bi-layer type arrangements that are frequently observed for a wide range of C[4]s.<sup>31</sup> The two crystallographically unique Mn-O and Mn-N bonds have distances as follows: Mn[1]-O[7], 2.121(2) Å; Mn[1]-O[8], 2.192(4) Å; Mn[1]-N[1], 2.283(4) Å. Symmetry expansion reveals that there is an interaction between one of the water of crystallisation and one carboxyl group, occurring with an H[5O]...O[10] distance of 1.788 Å. In addition to this there are several interactions between the other disordered water molecules and another carboxyl group with O...O distances ranging from 2.589 – 2.826 Å. There is also a CH...O interaction between another carboxyl group and the disordered methanol in both positions, with distances between 2.733 – 3.061 Å.



**Figure 7.** Partial extended structure of **8** showing neighbouring the coordination polymer chain formed by the octahedral Mn(II) centres and di-anionic calixarenes. Selected atoms have been labelled according to discussion. The disordered methanol and pyridines are shown in one of two positions and hydrogen atoms have been omitted for clarity.

An analogous synthetic procedure that was used to generate **8** was carried out using  $\text{Co}(\text{NO}_3)_2$  as the metal salt in place of  $\text{Mn}(\text{NO}_3)_2$ . Slow evaporation over several weeks resulted in the formation of pale pink plates suitable for X-ray diffraction

studies. Unit cell dimensions for this cobalt coordination polymer, **9**, were similar to those of **8**, suggesting that these are isostructural. Unfortunately we found crystals of **7** – **9** to degrade upon removal from the mother liquor for relatively short periods of time, suggesting that additional approaches are required in order to afford stable metal-organic assemblies that may prove useful for the study of selective guest uptake in the C[4] cavities, for example.

## Conclusions

$p\text{CO}_2[4]$ s have been shown to be versatile building blocks for use in supramolecular chemistry in the presence of pyridine (or pyridine-based) **guest templates**. Compound **4** incorporates two short diethylene glycol units that restrict conformation flexibility, keeping the molecule locked in the cone conformation and the cavity permanently accessible to guest molecules. The structures presented in this study show a tendency for the upper-rim carboxyl groups to form  $\text{Py}\cdots\text{CO}_2\text{H}$  heterosynthons rather than  $\text{CO}_2\text{H}\cdots\text{CO}_2\text{H}$  homosynthons which is in line with precedent. This **guest template** behaviour was expanded to include salt and related heterosynthon formation when 2-AP was employed. Initial exploration of the coordination chemistry of this new  $p\text{CO}_2[4]$  bis-crown afforded a small series of 1-D coordination polymers that were not stable towards de-solvation / removal from the mother liquor. Although this is the case, this building block may find further utility in the assembly of higher-dimensionality CPs and coordination cages when a broader study of its supramolecular chemistry is undertaken. Future work will focus on the use of directing fragments to synthesise such species and investigate their stability towards de-solvation / guest exchange, as well as the selective extension and / or positioning of the upper-rim carboxyl functionalities with a view to altering the self-assembly behaviour of this 'rigidified' calix[4]arene framework.

## Notes and references

### Experimental

Compounds **1**<sup>34</sup> and **2**<sup>28</sup> were synthesised according to literature procedure and purity checked by  $^1\text{H}$  NMR prior to use in subsequent steps. Reagents were purchased from chemical suppliers (Alfa Aesar, Fisher Scientific and Sigma Aldrich) and used as received. Electrospray ionisation and Fourier transform mass spectra (ESI-FTMS) were obtained on a LTQ Orbitrap XL spectrometer at the EPSRC National Mass Spectrometry Service centre at Swansea University.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on Bruker AC 300 and Bruker AC 400 spectrometers, with chemical shifts reported in ppm with respect to TMS as an internal standard. IR spectra were acquired on a Perkin Elmer Spectrum 100 FT-IR Spectrometer, with wavenumber ( $\nu$ ) of absorption reported in  $\text{cm}^{-1}$ . Single crystals were analysed on either a Bruker Apex II CCD diffractometer (for **6**) operating at 100(2) K with Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å) with a graphite monochromator or a Bruker Apex II CCD diffractometer (for **5**, **7** and **8**) operating at

100(2) K with synchrotron radiation ( $\lambda = 0.77490 \text{ \AA}$ ). H atoms were placed at geometrically calculated positions in **5–8**.

**Synthesis of 5,11,27,23-tetraformylcalix[4]arene-25,26,27,28-bis-crown-3 (3):** Compound **2** (1.00 g, 1.77 mmol) and HMTA (8.99 g, 0.06 mol) were dissolved in TFA (50 mL) and heated at reflux for 48 h. The hot reaction was poured onto ice water (50 mL) and stirred for 30 mins before the product was extracted into DCM (2 X 100 mL) and the organic layer was washed with water (2 X 100 mL), dried ( $\text{MgSO}_4$ ) and the solvents evaporated to give compound **46** as a pale yellow solid (1.00 g, 83%).  $^1\text{H NMR}$  (300 MHz, 25 °C,  $\text{CDCl}_3$ ):  $\delta = 9.72$  (s, 4H, CHO), 7.58 (d,  $J = 2.6$  Hz, 4H, ArH), 7.52 (d,  $J = 2.6$  Hz, 4H, ArH), 5.02 (d,  $J = 12.4$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 4.50 (d,  $J = 12.4$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 4.22 (m, 12H,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.88 (m, 4H,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.35 (m, 4H,  $\text{ArCH}_2\text{Ar}$ ).  $^{13}\text{C NMR}$  (300 MHz, 25 °C,  $\text{CDCl}_3$ ):  $\delta = 191.29, 191.07, 160.59, 135.00, 135.79, 132.75, 131.20, 130.36, 77.24, 76.39, 74.12, 30.58, 29.71$ . IR (solid phase,  $\nu \text{ cm}^{-1}$ ) = 2920m, 2873m, 1605s, 1463s, 1286s, 1081m. MS  $m/z$  observed 694.2639, theoretical 694.26347 [ $\text{M} + \text{NH}_4$ ] $^+$ .

**Synthesis of 5,11,27,23-tetracarboxylatocalix[4]arene-25,26,27,28-biscrown-3 (4):** A 50 mL round bottom flask was charged with a solution of compound **3** (0.27 g, 0.48 mmol) dissolved in DCM (5 mL) and acetone (15 mL) prior to the addition of aqueous solutions of  $\text{NaClO}_2$  (0.35 g, 3.87 mmol in 5 mL of water) and sulfamic acid (0.38 g, 3.87 mmol in 5 mL of water). The mixture was left to stir at room temperature overnight before removal of the organic solvents under reduced pressure to afford compound **4** as a yellow solid that was filtered, washed with water and air dried (0.27 g, 88%).  $^1\text{H NMR}$  (300 MHz, 25 °C,  $\text{DMSO-d}_6$ ):  $\delta = 12.51$  (s, 4H, COOH), 7.73 (s, 8H, ArH), 5.00 (d,  $J = 12.0$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 4.45 (d,  $J = 12.0$  Hz, 2H,  $\text{ArCH}_2\text{Ar}$ ), 4.19 (m, 12H,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.62 (m, 4H,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.45 (m, 4H,  $\text{ArCH}_2\text{Ar}$ ).  $^{13}\text{C NMR}$  (300 MHz, 25 °C,  $\text{DMSO-d}_6$ ):  $\delta = 166.68, 159.19, 135.48, 135.46, 130.48, 129.70, 126.15, 76.55, 73.71, 29.44, 28.86$ . IR (solid phase,  $\nu \text{ cm}^{-1}$ ) = 2924m, 1682s, 1603m, 1423m, 1279s, 1196s. MS  $m/z$  observed 758.2446, theoretical 758.2443 [ $\text{M} + \text{NH}_4$ ] $^+$ .

**†Crystal data for 5 (CCDC 1948423):**  $\text{C}_{64}\text{H}_{64}\text{N}_4\text{O}_{14}$ ,  $M = 1113.19$ , colourless block,  $0.13 \times 0.02 \times 0.02 \text{ mm}^3$ , orthorhombic, space group  $Pna2_1$ ,  $a = 32.470(2)$ ,  $b = 16.2657(9)$ ,  $c = 10.7306(6) \text{ \AA}$ ,  $V = 5667.4(5) \text{ \AA}^3$ ,  $Z = 4$ , Bruker Apex II CCD diffractometer, Synchrotron radiation,  $\lambda = 0.77490 \text{ \AA}$ ,  $T = 100(2)\text{K}$ ,  $2\theta_{\text{max}} = 55.7^\circ$ , 71067 reflections collected, 10395 unique ( $R_{\text{int}} = 0.0598$ ). Final  $\text{Goof} = 1.018$ ,  $R = 0.0404$ ,  $wR = 0.0988$ ,  $R$  indices based on 8994 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ).

**Crystal data for 6 (CCDC 1948424):**  $\text{C}_{60}\text{H}_{68}\text{N}_8\text{O}_{18}$ ,  $M = 1189.22$ , colourless block,  $0.40 \times 0.35 \times 0.30 \text{ mm}^3$ , monoclinic, space group  $P2_1/n$ ,  $a = 17.772(2)$ ,  $b = 11.657(1)$ ,  $c = 29.512(3) \text{ \AA}$ ,  $\beta = 101.183(3)^\circ$ ,  $V = 5998.0(11) \text{ \AA}^3$ ,  $Z = 4$ , Bruker Apex II CCD diffractometer, Mo- $\text{K}\alpha$  radiation,  $\lambda = 0.71073 \text{ \AA}$ ,  $T = 100(2)\text{K}$ ,  $2\theta_{\text{max}} = 41.62^\circ$ , 40470 reflections collected, 6251 unique ( $R_{\text{int}} = 0.1060$ ). Final  $\text{Goof} = 1.017$ ,  $R = 0.0883$ ,  $wR = 0.2817$ ,  $R$  indices based on 3790 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ).

#### Synthesis of coordination polymers

As stated above, these reactions were carried out in a range of metal salt stoichiometries relative to compound **4**, with three experiments forming single crystals as reported here.

**Synthesis of 7:** A mixture of compound **4** (0.10 g, 0.13 mmol) suspended in methanol (2 mL) was added to a methanolic solution of  $\text{Cu}(\text{NO}_3)_2$  (67.0 mg, 0.28 mmol dissolved in 2 mL of methanol). Gentle heating followed by dropwise addition of Py resulted in a clear solution being obtained. Slow evaporation over several weeks resulted in the formation of green/blue blocks suitable for X-ray diffraction studies. **Crystal data for 7 (CCDC 1948425):**  $\text{C}_{55}\text{H}_{49}\text{N}_3\text{O}_{14}\text{Cu}_1$ ,  $M = 1039.51$ , green block,  $0.06 \times 0.05 \times 0.05 \text{ mm}^3$ , orthorhombic, space group  $C222_1$ ,  $a = 14.8977(4)$ ,  $b = 29.2369(9)$ ,  $c = 12.7603(5) \text{ \AA}$ ,  $V = 5557.9(3) \text{ \AA}^3$ ,  $Z = 4$ , Bruker Apex II CCD diffractometer, Synchrotron radiation,  $\lambda = 0.77490 \text{ \AA}$ ,  $T = 100(2)\text{K}$ ,  $2\theta_{\text{max}} = 51.76^\circ$ , 31696 reflections collected, 4170 unique ( $R_{\text{int}} = 0.0499$ ). Final  $\text{Goof} = 1.065$ ,  $R = 0.0654$ ,  $wR = 0.1843$ ,  $R$  indices based on 3763 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ).

**Synthesis of 8:** An analogous procedure to that used in the synthesis of **7** was carried out using  $\text{Mn}(\text{NO}_3)_2$  (0.10 g, 0.55 mmol) as the metal salt. Slow evaporation over several weeks resulted in the formation of orange blocks suitable for X-ray diffraction studies. **Crystal data for 8 (CCDC 1948426):**  $\text{C}_{57}\text{H}_{65}\text{N}_3\text{O}_{20}\text{Mn}_1$ ,  $M = 1167.06$ , orange block,  $0.13 \times 0.05 \times 0.03 \text{ mm}^3$ , monoclinic, space group  $C2/c$ ,  $a = 12.4398(5)$ ,  $b = 27.984(1)$ ,  $c = 15.9403(6) \text{ \AA}$ ,  $\beta = 91.647(2)^\circ$ ,  $V = 5546.8(4) \text{ \AA}^3$ ,  $Z = 4$ , Bruker Apex II CCD diffractometer, Synchrotron radiation,  $\lambda = 0.77490 \text{ \AA}$ ,  $T = 100(2)\text{K}$ ,  $2\theta_{\text{max}} = 58.06^\circ$ , 35944 reflections collected, 5701 unique ( $R_{\text{int}} = 0.0440$ ). Final  $\text{Goof} = 1.040$ ,  $R = 0.0852$ ,  $wR = 0.2733$ ,  $R$  indices based on 4310 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ).

**Synthesis of 9:** An analogous procedure to that used in the synthesis of **7** was carried out using  $\text{Co}(\text{NO}_3)_2$  (0.16 g, 0.55 mmol) as the metal salt. Slow evaporation over several weeks resulted in the formation of pale pink plates suitable for X-ray diffraction studies. Unit cell dimensions for **9** ( $a = 12.4039$ ,  $b = 27.9274$ ,  $c = 15.9504$ ,  $V = 5523.84 \text{ \AA}^3$ ) revealed these crystals to be isostructural to **8**.

#### Conflicts of interest

There are no conflicts to declare.

#### Acknowledgements

We thank EPSRC for financial support of this work through a DTP studentship for REF and provision of Mass Spectrometry analysis at Swansea University. We also thank the Royal Society Newton Mobility Fund for supporting this collaboration (IL / SJD) under grant reference NI170151. The Advanced Light Source is supported by the Director, Office of Science, Office of Basic Energy Sciences, of the US Department of Energy under contract no. DE-AC02-05CH11231.

- 1 V. Bohmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713.
- 2 T. Michinori and S. Seiji, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 1088.
- 3 J. Wu and Y. Yang, *Chem. Commun.*, 2019, **55**, 1533.
- 4 For further examples of widespread application please see: M. Luigi and U. Rocco, *Calixarenes In Action*, Imperial College Press, London, 2000.

- 5 For recent examples please see: P. Neri, J. L. Sessler and M. X. Wang *Calixarenes and Beyond*, Springer International Publishing, Switzerland, 2016.
- 6 C.D. Gutsche, *Calixarenes: An Introduction: Edition 2*, The Royal Society of Chemistry, Cambridge, 2008.
- 7 Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, *Calixarenes 2001*, Kluwer Academic Publishers, 2001.
- 8 C. D. Gutsche, Chapter 4 in *Calixarenes Revisited*; J. F. Stoddart, Ed., The Royal Society of Chemistry: Cambridge, 1998.
- 9 A. Arduini, M. Fabbi, M. Mantovani, L. Mirone, A. Pochini, A. Secchi and R. Ungaro, *J. Org. Chem.*, 1995, **60**, 1454.
- 10 S. Kennedy, C. M. Beavers, S. J. Teat and S. J. Dalgarno, *CrystEngComm*, 2014, **16**, 3712.
- 11 P. P. Cholewa and S. J. Dalgarno, *CrystEngComm*, 2014, **16**, 3655.
- 12 S. J. Dalgarno, J. E. Warren, J. Antesberger, T. E. Glass and J. L. Atwood, *New. J. Chem.* 2007, **31**, 1891.
- 13 For example see: P. Vishweshwar, A. Nangia, V. M. Lynch, *J. Org. Chem.*, 2002, **67**, 556.
- 14 S. Kennedy, S. J. Teat and S. J. Dalgarno, *Dalton Trans.*, 2010, **39**, 384; S. Kennedy, C. M. Beavers, S. J. Teat and S. J. Dalgarno, *Cryst. Growth Des.* 2012, **12**, 679; S. Kennedy, I. E. Dodgson, C. M. Beavers, S. J. Teat and S. J. Dalgarno, *Cryst. Growth Des.* 2012, **12**, 688.
- 15 S. Kennedy and S. J. Dalgarno, *Chem. Commun.*, 2009, 5275.
- 16 S. Kennedy, C. M. Beavers, S. J. Teat and S. J. Dalgarno, *New. J. Chem.* 2011, **35**, 28.
- 17 S. Kennedy, P. Cholewa, R. D. McIntosh and S. J. Dalgarno, *CrystEngComm.*, 2013, **15**, 1520.
- 18 L. G. Kuz'mina, G. G. Sadikov, J. A. K. Howard, E. A. Shokova and V. V. Kovalev, *Kristallografiya*, 2003, **48**, 272.
- 19 P. P. Cholewa, C. M. Beavers, S. J. Teat, S. J. Dalgarno, *Cryst. Growth Des.*, 2013, **13**, 5165.
- 20 P. P. Cholewa, C. M. Beavers, S. J. Teat, S. J. Dalgarno, *Chem. Commun.*, 2013, **49**, 3203.
- 21 S. Pasquale, S. Sattin, E. C. Escudero-Adán, M. Martínez-Belmonte, J. de Mendoza, *Nat. Commun.*, 2012, **3**:785, 1793.
- 22 A. Pochini, and R. Ungaro, *Comprehensive Supramolecular Chemistry*; F. Vögtle, Ed.; Elsevier: New York, 1996.
- 23 W. Sliwa, and C. Kozłowski, *Calixarenes and Resorinarenes: Synthesis, Properties and Applications*, Wiley-VCH, Weinheim, 2009.
- 24 C. Alfieri, E. Dradi, A. Pochini, R. Ungaro and G. D. Andreotti, *J. Chem. Soc., Chem. Commun.*, 1983, 1075.
- 25 A. Arduini, A. Casnati, L. Dodi, A. Pochini and R. Ungaro, *J. Chem. Soc., Chem. Commun.*, 1990, 1597
- 26 A. Arduini, L. Domiano, A. Pochini, A. Secchi, R. Ungaro, F. Ugozzoli, O. Struck, W. Verboom and D. N. Reinhoudt, *Tetrahedron*, 1997, **53**, 3767.
- 27 S. Caccmese, A. Notti, S. Pappalardo, M. F. Parisi and G. Principato, *Tetrahedron*, 1999, **55**, 5505.
- 28 A. Arduini, W. M. McGregor, D. Paganuzzi, A. Pochini, A. Secchi, F. Ugozzoli and R. Ungaro, *J. Chem. Soc., Perkin Trans. 2*, 1996, 839.
- 29 V. Arora, H. M. Chawla and A. Santra, *Tetrahedron*, 2002, **58**, 5591.
- 30 Q. Lin and A. D. Hamilton, *C. R. Chimie.*, 2002, **5**, 441.
- 31 S. Kennedy, G. Karotsis, C. M. Beavers, S. J. Teat, E. K. Brechin, S. J. Dalgarno, *Angew. Chem. Int. Ed.*, 2010, **49**, 4205.
- 32 For an example of a *p*-tert-butylcalix[4]arene bi-layer assembly see: J. L. Atwood, L. J. Barbour, A. Jerga and B. L. Schottel, *Science*, 2002, **298**, 1000.
- 33 A. L. Spek, *Acta Crystallogr. A*, 1990, **46**, C34.
- 34 M. Cui, X. Wang, P. Yu, J. Zhang, Z. Li, X. Zhang, Y. Yang, M. Ono, H. Jia, H. Saji and B. Liu, *J. Med. Chem.* 2012, **55**, 9283.