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Forbidden Crystals:
Penrose Tiling With Molecules

A thesis submitted in partial fulfilment of the requirements
for the degree of Doctor of Philosophy in Chemistry,
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Abstract

Since the first discovery of 3D quasicrystals observed by Daniel Shechtman, the concept of long-range aperiodic crystallinity has become intriguing to numerous scientists. This thesis describes the extension of the quasicrystal concept to two-dimensions, using 5-fold symmetric molecules to explore molecular Penrose tiling.

Chapter 1 covers the history and current interest of quasicrystals. Penrose tiling is introduced as a geometrical model for 2D quasicrystalline ordering. Examples of reported approaches to molecular Penrose tiling are described. The design concept used in this thesis (5*-., 3*- and 2*-molecular pentagons substituted with the corresponding number of linkers) is established.

Chapter 2 describes the syntheses and characterisation of several series of molecular pentagons. The candidates are croconate family, cyanocyclopentadienyls, campestarenes, Singapore Pentamers and cucurbit[5]urils. The synthetic approaches and difficulties encountered are discussed and resolutions presented. In particular, substitution of those molecular pentagons with appropriate linkers are intensively discussed.

Chapter 3 describes the production and characterisation of Au(111) substrates. The production includes preparation of parent substrates, thermal evaporation of gold and cleaning process. The gold substrates prepared in this thesis are characterised using XPS, XRD, EBSD and AFM.

Chapter 4 presents the deposition of the synthesised molecular pentagons on a surface and characterisation of the deposited monolayers by high resolution STM and AFM. This study was carried out in collaboration with Dr. Haifeng Ma at The University of Canterbury, Prof. Amar Flood and Prof. Steve Tait at Indiana University and Prof. Ronan McGrath at The University of Liverpool.

Chapter 5 contains the summary of this thesis and future work. Experimental procedures are detailed in Chapter 6.
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<th>Description</th>
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<tbody>
<tr>
<td>Å</td>
<td>Ångström</td>
</tr>
<tr>
<td>AFM</td>
<td>atomic-force microscopy</td>
</tr>
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<td>aq</td>
<td>aqueous</td>
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<td>HMBC</td>
<td>heteronuclear multiple bond correlation</td>
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<tr>
<td>HOPG</td>
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<td>HPLC</td>
<td>high performance liquid chromatography</td>
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<td>HSQC</td>
<td>heteronuclear single quantum correlation</td>
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<td>HRMS</td>
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<tr>
<td>IR</td>
<td>infrared</td>
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<td>J</td>
<td>coupling constant</td>
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<td>LEED</td>
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<td>m</td>
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<tr>
<td>M</td>
<td>mol L(^{-1})</td>
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<tr>
<td>MALDI</td>
<td>matrix-assisted laser desorption ionization</td>
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List of abbreviations continued

<table>
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<th>Abbreviation</th>
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<tr>
<td>MeOH</td>
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<tr>
<td>SP</td>
<td>Singapore Pentamer</td>
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<tr>
<td>STM</td>
<td>scanning tunneling microscope</td>
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<tr>
<td>td</td>
<td>triplet of doublets</td>
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<td>ultraviolet</td>
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<tr>
<td>v</td>
<td>stretching frequency</td>
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<tr>
<td>XPS</td>
<td>X-ray Photoelectron Spectroscopy</td>
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<tr>
<td>XRD</td>
<td>X-ray powder diffraction</td>
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Chapter 1  Introduction

1.1 Penrose tiling and Quasicrystals

Classically, two dimensional tiling is usually achieved by use of triangular, square or hexagonal tiles which can completely cover a surface, leaving no gaps. Compared to those Archimedean tilings which are periodic arrangements of regular polygons laid edge-to-edge in a plane, pentagons cannot completely fill spaces without overlaps. Tilings with pentagons require other shapes. Girih patterns which are geometric star-and-polygon, or strapwork were found in medieval Islamic architecture. Figure 1.1 is an example of an Islamic architecture where the tilings are filled with decagons, hexagons, bowties, and rhombuses. These aperiodic tilings with 5-fold and/or 10-fold symmetric motifs found in Islamic architecture could be the first two dimensional quasicrystalline patterns.

![Figure 1.1. The octagonal Gunbad-i Kabud tomb tower in Maragha, Iran (1197 C.E.), with the girih-tile reconstruction of one panel overlaid (left) and close-up of the area (right) (reproduced from ref. 1).](image)

The first descriptions of these tiling patterns were in 1619 by Johannes Kepler. In his book, packings of polygons in the plane including the Penrose tiling architecture comprising pentagon, rhombus, star and decagon instead of crown, were described (Figure 1.2 in blue circle). Marjorie Senechal also
studied geometries of aperiodic tilings including those Kepler discovered. By filling up the decagons
with three pentagons, a crown and a rhombus, Kepler’s structure translates to Penrose tiling.

Figure 1.2. Kepler’s experiments with polygon packings. The Penrose tiling architecture is in blue
circle (reproduced from ref. 3).

In the 1970s the mathematician Roger Penrose investigated Penrose tilings. These comprise a surface
covered by pentagonal shapes without overlaps exhibiting localized five-fold rotational symmetry but
they are translationally non-periodic. Unlike the use of triangles, squares or hexagons, Penrose tiling
requires the use of more than one shape, either rhombic or pentagonal. Figure 1.3 shows the Penrose
tiling pattern consisting of pentagon, rhombus, crown and star tiles. Kite and dart tiling and rhombus
tiling are other types of aperiodic tiling shown in Figure 1.4. These patterns lack translational
symmetry which means that a shifted copy will never match the original.
Figure 1.3. Penrose tiling pattern.

Figure 1.4. a) Kite and dart Penrose tiling and its two components (reproduced from ref. 5) and b) fat and thin rhombus tiling, with one example of each of the seven different types of node in a circle and its two components (reproduced from ref. 6).
Three dimensional aperiodic crystals are named quasicrystals and their periodicity is called quasi-periodicity. They can be considered to be a three dimensional manifestation of Penrose tiling. In 1984 Dan Shechtman (the 2011 Nobel Prize laureate in chemistry) and co-workers\textsuperscript{7} reported that alloys of Al with 10-14 atom \% Mn diffracted not only like a single crystal, but also exhibited icosahedral symmetry in a selected area which was inconsistent with lattice translations. The electron diffraction pattern showed sharp reflections with 10-fold symmetry. This discovery precipitated a paradigm shift in crystallography in which 5-fold symmetry was previously thought to be not attainable.

Figure 1.5. 10-fold symmetry of Al-Mn alloy diffraction (reproduced from ref. 9).

Further structural, physical and crystallographic studies of quasicrystals in metallic alloys have been reported. Based on their theoretical and physical studies of quasicrystals, Levine and Steinhardt reported that quasicrystals possess a wealth of remarkable new structural and electronic properties.\textsuperscript{8} Steurer and Deloudi defined quasicrystals \textit{via} crystallographic analyses of various metallic alloys.\textsuperscript{9} Mehl in 2005\textsuperscript{10} investigated self-assembling behaviours of soft materials, such as dendrimers and copolymers, showing that the quasi-crystalline pattern with 12-fold symmetry was also observed in these materials. Quasicrystalline behaviour is often observed for 5-, 10- and 12-fold symmetry. This suggested that quasiperiodicity is not restricted to intermetallic phases and electron stabilisation is not a necessary requirement. A variety of structural studies in transition metal systems as well as in soft matter have been reported. Such quasiperiodic structures exist in scaled-up micellar phases, indicating a soft matter mode.\textsuperscript{11}

Metallic alloy quasicrystals have unusual magnetic,\textsuperscript{12} frictional,\textsuperscript{13} catalytic,\textsuperscript{14} and optical properties.\textsuperscript{15} It is considered that the correlation between chemical structure and physical properties is the major factor for the unusual properties, and interest in their properties is growing.\textsuperscript{16} For example, icosahedral quasicrystals have been used as materials for photonic circuits.\textsuperscript{17}
1.2 Creating Penrose tiling on a surface

1.2.1 Examples of general Penrose tilings

Tools of lasers and nanotechnology have been used to successfully generate two-dimensional aperiodic tilings in materials. A Penrose-like template has been achieved on monolayers of mono-disperse silica beads in good quality through electron beam lithography (Figure 1.6).\textsuperscript{18} The organised silica beads prepared on Penrose-patterned substrates by dip-coating processes have been investigated by AFM techniques and SEM imaging.\textsuperscript{19} This Penrose-template technique potentially leads to silica photonic materials that produces large frequency band gaps. In addition, a colloidal monolayer created by interfering five laser beams on a quasicrystalline decagonal substrate has been reported.\textsuperscript{16b} A pseudomorphic phase from the colloidal monolayer which can be described by an Archimedean-like tiling has both crystalline and quasicrystalline structural properties.

![AFM imaging of a Penrose-like template on Si substrates. In inset 2D calculated Fast Fourier Transform (FFT) (reproduced from ref. 18).](image)

1.2.2 Examples of molecular Penrose tilings

Molecular quasicrystals have recently been intriguing since three publications of the production of molecular quasicrystals in monolayers appeared in early 2014 by Ronan McGrath,\textsuperscript{20} Vincent Fournée\textsuperscript{21} and Alex Kandel.\textsuperscript{22} Alex Kandel and Ronan McGrath’s work was highlighted in Nature Nanotechnology, titled “Quasicrystals, Now in molecular layers” in April 2014.\textsuperscript{23}
The first attempt to create molecular quasicrystals was reported in 2009. Bauert and co-workers deposited corannulene and its chiral penta-substituted derivatives, which have C5 and C5v symmetries on Cu(111) substrates. However, these “Buckybowls” (Figure 1.7a) on Cu(111) appeared in hexagonal close-packing ordered by underlying symmetry of the Cu(111) surface. Pentachloro- (Figure 1.7b) and pentamethyl- (Figure 1.7c) corannulenes created a slight star-like form in random orientations with positional disorder. The major reason that the arrangements of Buckybowl and its derivatives did not form Penrose tilings is probably that there is no means of controlling the edge-edge interactions to achieve the ordering.

![Buckybowl and cartoons from STM images of (a) Buckybowl and (b) its pentachloro- and (c) pentamethyl- derivatives on Cu(111) (reproduced from ref. 24).](image)

McGrath’s group used quasicrystalline templates and on these deposited organic molecules such as pentacene (Pn) and fullerene (C60) without any interaction between molecules. His group varied the quasicrystalline templates, such as AlPdMn and AlNiCo, and deposition temperatures for fullerene and pentacene. Deposition of C60 on face-centered icosahedral AlCuFe at 773 to 973 K and pentacene on simple icosahedral AgInYb at 300 K was successful in creating quasicrystalline monolayers, published in 2014 (Figure 1.8). This is the first achievement of production of molecular Penrose tiling.
Figure 1.8. a) STM images (left) and the resultant autocorrelation image (right) of quasicrystalline C\textsubscript{60} layer on icosahedral Al–Cu–Fe and b) pentacene positions extracted and plotted (left) with and (right) without orientation information from a quasicrystalline pentacene layer on icosahedral Ag–In–Yb. The autocorrelation functions in the lower figure show the increased quality of the quasicrystalline ordering when the orientation of the pentacene molecules is included (reproduced from ref. 20).

Fournée and his colleagues also reported templated self-ordering of fullerene (C\textsubscript{60}) in a long-range quasiperiodic order in 2014.\textsuperscript{21} C\textsubscript{60} was evaporated onto AlPdMn, AlCuFe, AlCoCu and AlNiCo quasicrystal templates at substrate temperatures ranging from 623 to 673 K. Quasicrystallinity of the molecular layers was observed by STM and LEED (Figure 1.9). Moreover, the absorption preference of C\textsubscript{60} on quasicrystalline sites of the templates was studied.
Kandel’s group reported the unexpected self-assembly of quasicrystals with ferrocenecarboxylic acid on Au(111) surfaces in 2014.\textsuperscript{22} Intermolecular hydrogen bonding between carboxylic acids as well as between the carboxylic acid hydrogen and the adjacent C-H on cyclopentadienyl rings allowed five ferrocenecarboxylic acids to assemble as a pentagon, shown in Figure 1.10b. Those pentagons were deposited parallel to the surface. Additional ferrocenecarboxylic acid dimers which were perpendicular to the surface glued together the ferrocenecarboxylic acid pentagons.\textsuperscript{25} This allowed ordering of the ferrocenecarboxylic acid pentagons in Penrose tiling patterns and fragments of molecular Penrose tiling was observed by STM as shown in Figure 1.10c. This serendipitous discovery of the self-assembly of pentamers was the first example of creating molecular Penrose tiling on a flat surface via intermolecular interactions.
Figure 1.10. a) Structure of ferrocenecarboxylic acid; b) STM image of the pentagons comprising of five ferrocenecarboxylic acids and ferrocenecarboxylic acid dimers between the pentagons; c) overlaid with pentagons showing fragments of the long-range quasicrystalline order; (b) and (c) were reproduced from ref. 22).

1.3 Design of molecular Penrose tiling

The above examples either used quasicrystalline alloy face as a template or were discovered serendipitously. Higher order is a challenge to achieve a two dimensional quasicrystal through rational design. A theoretical approach to designing molecular quasicrystals used 10-fold symmetric coronenes with substitution patterns designed to mimic the seven different nodes in the rhombus Penrose tiling. The carboxylic acid substituted 10,5-coronenes would be linked through hydrogen-bonded bridges
Moreover, a simplified three component approach was reported. However, synthetic accessibility of tiles is the major concern. Synthesis of coronene and its family has not been reported and these synthetic drawbacks were the major obstacle to developing the molecular Penrose tiling with coronene. In addition to the coronene family, other potential candidates as tiles corannulene derivatives like pentaiminocorannulene have not yet been realised experimentally. Even more complicated organic molecules as tiles have been designed and computationally calculated for rhombus tiling but the syntheses of those molecules are not practically possible.

![Figure 1.11](image1.png)

Figure 1.11. a) Penrose tiling, with one example of each of the seven different types of node in a circle (reproduced from ref. 3); and b) an example of a molecule from the coronene family.

![Figure 1.12](image2.png)

Figure 1.12. Pentaiminocorannulene.

Synthetically accessible 5-fold symmetric molecules are cyano-substituted cyclopentadienyls, croconate, macrocycles based on expanded porphyrins (pentaphyrins, rosarin and isoamethyrins), other new planar pentagonal macrocycles (campestarenes, macrocycle pentamers and cyanostars)
and supramolecular building blocks (calix[5]arenes, \cite{37} [5]cavitands, \cite{38} metallacyclopahanes, \cite{39} pentafoil knots, \cite{40} cucurbit[5]urils\cite{41}). In this project, croconate, cyano-substituted cyclopentadienyls, \cite{30} campestarenes, \cite{34} macrocycle pentamers\cite{35} and cucurbit[5]urils\cite{41} are investigated.

We propose a new approach to analyzing the pentagonal Penrose tiling pattern that comprises pentagon, rhombus, star and crown. The analysis of Penrose tiling pattern shows in Figure 1.13 that three pentagonal components are sharing 5, 3 and 2 edges, denoted 5*, 3* and 2*, respectively. A closer analysis of Figure 1.13 shows that the 5* tiles link only with 3* or 2* tiles and direct links between two tiles of the same type (5*-5*, 3*-3* or 2*-2*) never occur. As detailed in Figure 1.14, the 3* tiles have two different edges, 3a and 3b, with the specific linkages: 3a-5* and 3b-2*. Shared edges of 2* tiles are not neighbours. The rhombus (r), star (s) and crown (c) shapes will occur as gaps between the pentagonal tiles.

![Figure 1.13. Penrose tiling. Pentagons sharing 5, 3 and 2 edges are denoted 5*, 3* and 2*, respectively; rhombus, star and crown gaps are denoted r, s and c, respectively.](image)
Appropriate selections of the substituents to use as linking groups are essential to create the edge-sharing rules. Two methods of linking tiles by the edge-sharing rules can be envisaged: a system where only one functional group (●) is used allowing ●-● recognition (Figure 1.15a), or two different groups leading to ●-○ recognition where ●-● or ○-○ links are not allowed, as in DNA base pairing (Figure 1.15b). Control of bonding-selectivity like 3*-3* (Figure 1.16) instead of 5*-3* or 2*-3* would be a challenge that would occur in the method of Figure 1.15a. Potential molecular recognition elements for both types could be, for example, cyano-silver-cyano, carboxylic acid-carboxylic acid, carboxylic acid-carboxylate or carboxylic acid-pyridine (Figure 1.17), using coordination and supramolecular chemistry to control the edge-edge interactions. In particular, selective non-covalent interactions like π-π stacking in supramolecular chemistry will be useful tools to control structures and further to achieve molecular Penrose tiling on surfaces.
1.4 Project goals

The overall goal of this project is to explore the Penrose tiling based on molecular pentagon motifs to produce 2D quasicrystalline structures. Specifically, design and syntheses of synthetically accessible, functionalised 5-fold symmetric molecules are the priority as a start point. The molecular tiles must be compatible with organisation on a surface to produce monolayers on atomically flat substrates and, further, able to be selectively substituted with 5, 3 or 2 functional groups as linkers. The molecules discussed in this project are cyclopentadienyl derivatives (croconates and cyano-substituted cyclopentadienyls), macrocycles (campestarene and macrocyclic pentamer) and supramolecular building blocks (cucurbit[5]urils). 4-Fold or 6-fold symmetric molecules which are less synthetically
demanding are used as model compounds to study supramolecular linkage between tiles and optimisation of syntheses conditions.

To produce quasicrystalline monolayers with molecules, optimisation of deposition conditions such as deposition methods, deposition phases, temperature, exposure time to substrates and use of optimum substrates for each category of the synthesised molecules should be carried out. As part of optimisation of deposition condition, production of atomically flat Au(111) substrates by evaporation, including pre-treatment, thermal evaporation, cleaning/recycling and characterisation are described. Up-to-date STM and AFM investigation of ordering of the synthesised 5-fold symmetric molecules deposited by thermal evaporation, immersing or droplet technique is presented. Model compounds are used for optimisation of deposition conditions and comparison with the tiles. Tile-substrate and tile-tile interactions are investigated.
Chapter 2  Synthesis of molecular pentagons

In this thesis 5-fold symmetric molecules are classified into three categories by different size scales of the tiles; monomeric molecules, macrocycles and supramolecular building blocks. All candidates must be synthetically approachable. As each candidate has a different size scale and synthetic complexity, suitable linkers for each tile will be selected. Known macrocycles which are relatively easy to synthesise but which do not bear the linker groups can be used for models for the deposition studies. Moreover, in the supramolecular building block category 6-fold symmetric congeners which are more easily prepared can be used to develop the synthetic methods for attachment of the linkers and for further investigation of surface deposition.

2.1 Cyclopentadienyl derivatives

The smallest candidates with 5-fold symmetry are cyclopentadienyl derivatives: croconate and cyanopentadienide anion. These molecules are tiles which will be linked to one another via metal coordination. Croconic acid, 1,2,4-cyclopentanetrione and cyclopent-4-ene-1,3-dione which are all commercially available are 5*--, 3*- and 2*-tiles, respectively (Figure 2.1). Squaric acid with 4-fold symmetry is used as a model compound which is also commercially available. Preparations of cyclopentadienides that have been reported are discussed in this chapter. The commercially available molecular tiles were purchased and synthetically accessible molecules (pentacyanocyclopentadienide anion and croconate derivatives) were prepared to have a library of the tiles available.

2.1.1 Croconate

The first candidate is croconic acid which contains a cyclopentene core with two hydroxyl groups adjacent to the double bond and three carbonyl groups on the remaining carbon atoms. Loss of protons from the hydroxyl groups in croconic acid produces stabilised aromatic and symmetric croconate ion. The silver croconate complex is known, used as precursor to the dimethylated croconate (4,5-dimethoxycyclopent-4-ene-1,2,3-trione). It is interesting that the carbonyls contributed to coordination to form mono- or bidentate complexes with copper and one of the carbonyls adjacent to the hydroxyls was also used for coordination with platinum and copper. Furthermore, the potential 3*- and 2*- derivatives, hydroxycyclopent-4-ene-1,3-dione, 1,2,4-cyclopentanetrione and
cyclopent-4-ene-1,3-dione, respectively, (Figure 2.1) are synthetically and even commercially accessible.\textsuperscript{47} After deprotonation croconic acid and its derivatives will form mono- or di-anionic species, which can be envisaged as the 5*- , 3*- and 2*- tiles.

\begin{center}
\includegraphics[width=\textwidth]{croconate.png}
\end{center}

Croconate and the derivatives in anion forms

These three tiles in their anion forms do not tend to coordinate through all the carbonyl sites. For example, the croconate dianion has to be linked with five of the 3*- or 2*- corresponding compounds. There have been no reports that crystals of croconate are using all the five coordinating sites in a linear formation through monodentate coordination. Therefore, the key to utilising all the binding sites to coordinate metals as linkers could be activation of the carbonyls towards coordination and lithium will be one of the possible options to activate the carbonyl sites.\textsuperscript{48}
2.1.1.1 Model study with squarate and croconate

Figure 2.2. a) Croconic acid, b) croconate, c) squaric acid and d) squarate.

Squaric acid is a 4-fold symmetric molecule comprised of two carbonyls and two hydroxyl groups. Similar to croconate, squarate is also shown equal distribution of negative charges over all the C-O bonds (Figure 2.2). These 4-fold and 5-fold symmetric molecules were used for a coordination study in order to investigate an intermolecular network system for Penrose tiling. \([\text{AgNa(C}_5\text{O}_5)(\text{H}_2\text{O})_2]_n, \text{CO-1}, [\text{Co(C}_4\text{O}_4)(\text{H}_2\text{O})_4]_n, \text{CO-2} \text{ and } [\text{Co(C}_5\text{O}_5)(\text{H}_2\text{O})_3]_n, \text{CO-3} \) were synthesised in this thesis due to our interest in investigating coordination geometry and surface deposition for this system.

Figure 2.3. ORTEP plot of \([\text{AgNa(C}_5\text{O}_5)(\text{H}_2\text{O})_2]_n, \text{CO-1}, \) showing the metal coordination spheres at 40\% thermal ellipsoids (reproduced from ref. 43a).

\([\text{AgNa(C}_5\text{O}_5)(\text{H}_2\text{O})_2]_n, \text{CO-1} \) was synthesised by following the literature preparation.\(^{43a}\) Slow addition of aqueous silver nitrate solution to aqueous disodium croconate in solution and overnight stirring in the dark gave a green solution which then was stored in a desiccator over CaCl\(_2\) for a few days to give
green crystals of CO-1 in Figure 2.3. Unusual bidentate coordination with silver and Ag-Ag-Ag and Na-(μ-H$_2$O)$_2$-Na-(μ-H$_2$O)$_2$ chains were observed. It will be interesting to investigate the ordering and coordination network of the solution phase of the AgNa-croconate complex (CO-1) in monolayers.

![Figure 2.4. X-ray crystal structures](image)

Metal coordination study of squaric acid and croconic acid was carried out using cobalt as a linker. A mixture of cobalt(II) acetate and squaric acid or croconic acid in aqueous solution stirred at room temperature gave noticeable acetic acid odour. After removal of solvents, recrystallization of the crude product from water afforded the cobalt(II) complexes in Figure 2.4 which turned out to correspond to the reported structures. X-ray crystallography structures of cobalt complexes (CO-2 and CO-3) showed linear polymeric architectures with a 1:1 ratio of cobalt to the ligand. The coordination sphere of the metal centres was octahedral which allowed hydrogen bonding between the linear polymers via the H$_2$O ligands on cobalt in both the structures of CO-2 and CO-3. In addition, π-stacking between the ligands contributed to the packing between the linear polymers of cobalt-ligand in both Figure 2.4a and Figure 2.4b.

In CO-2, squarate coordinated to cobalt through the two non-adjacent oxygens and the C-O-Co bond angle was 133.49°. This monodentate coordination allowed quite ordered linear polymerisation. However, both monodentate and bidentate coordination were observed in the Co-croconate complex CO-3. One monodentate coordination from each croconate was found via one carbonyl and the C-O-Co bond angle was 143.23°. The oxygens adjacent to this carbonyl did not coordinate to the metal. The
two oxygens opposite the monodentate-coordinated oxygen formed a bidentate coordination site where the C-O-Co bond angles were 107.47° and 108.65°. Due to a mixture of the monodentate and bidentate coordination between cobalt and croconate, the geometry of Co-croconate polymer was less linear and adopted a slight zigzag form.

The planar structures of squarate and croconate are probably suitable for “flat” deposition on substrates rather than “edge-on” deposition unless there is an interaction between oxygens on squarate or croconate and the surface. If the reaction of metal with croconate is carried out under pressure and heat, all the carbonyls on croconate can be activated to become binding sites. In spite of these optimistic results, Penrose tiling of metal-croconate coordination has two drawbacks; non-linear bonding of metal-oxygen-carbon and no means of controlling bidentate coordination. All the C-O-metal bond angles observed Figure 2.4b are between 143.23° and 108.65° which will generate mixed binding in a random direction between tiles in 2D layers and therefore quasicrystalline lattice will be unlikely to form. In addition, the bidentate coordination tendency of croconate will complicate ordering of the croconate tiles in monolayers.

2.1.1.2 Croconate derivatives: 3* and 2*

1,2,4-cyclopentanetrione (CO-4) is the 3* tile which is commercially available. This molecule can also be synthesised via a reaction of diethyl 3-oxopentanedioate with diethyl oxalate in basic condition to yield diethyl 2,4,5-trioxocyclopentane-1,3-dicarboxylate which loses diethyl ester using concentrated hydrochloric acid to give 1,2,4-cyclopentanetrione (CO-4) as shown in Scheme 2.1.

![Scheme 2.1. Reaction scheme for the synthesis of 1,2,4-cyclopentanetrione (CO-4).](https://example.com/scheme2.1)

1,2,4-cyclopentanetrione (CO-4), which is not flat due to the presence of the sp³ carbons, can be flattened after losing two protons as shown Figure 2.5a. In contrast to the pKₐ values for croconate, which are 0.80 for the first proton and 2.24 for the second proton, the pKₐ of 1,2,4-cyclopentanetrione (CO-4) is 3.0 for the first proton and the second proton pKₐ has not yet been reported but must be much higher than 3. Sheley has reported that removal of the second proton of 1,2,4-cyclopentanetrione (CO-4) was extremely hard and the existence of CO-5 was still ambiguous since
the monosodium salt intermediate produced by deprotonation using sodium hydride was insoluble in DMF and did not undergo further reaction with sodium hydride.\textsuperscript{42a}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure25.png}
\caption{a) dianion forms of 1,2,4-cyclopentanetrione (CO-5), 3,5-diphenylcyclopentane-1,2,4-trione (CO-6) and b) resonance forms of 3,5-diphenylcyclopentane-1,2,4-trione (CO-6).}
\end{figure}

An alternative 3*-tile, 3,5-diphenylcyclopentane-1,2,4-trione (CO-7) was synthesised in 29\% yield by following the literature preparation (Scheme 2.2).\textsuperscript{42b} The synthesis of 3,5-diphenylcyclopentane-1,2,4-trione (CO-7) was achieved by a one-step reaction in which 1,3-diphenylpropan-2-one reacted with diethyl oxalate and sodium ethoxide in ethanol, followed by protonation using 2 N sulfuric acid. CO-7 could react with sodium carbonate and a stronger base like sodium hydride to form yellow monoanion and a purple oil as CO-6. This was due to the two electron-donating phenyl groups, which stabilised the very reactive dianion compound. Although the diphenyl dianion species was still so reactive that it reacted with water in the air and turned back to the monoanion salt, the diphenyl dianion species was produced, isolated and is usable for further studies. Contribution of the phenyl rings to stabilisation of the diphenyl dianion species via resonance is as shown Figure 2.5b

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{scheme22.png}
\caption{Reaction scheme for the synthesis of 3,5-diphenylcyclopentane-1,2,4-trione, CO-7.\textsuperscript{42b}}
\end{figure}
Cyclopent-4-ene-1,3-dione (CO-8) and 2-methyl-1H-indene-1,3(2H)-dione (CO-9) are 2* tile candidates. They are both commercially available. The synthesis of CO-9 was a one-step reaction described in the literature.\textsuperscript{42c} Therefore, CO-9 was synthesised \textit{via} a reaction of dimethyl phthalate with 3-pentaneone and sodium hydride in toluene to give the anionic product which was acidified with concentrated hydrochloric acid to give yellow solid products in quantitative yield (Scheme 2.3). After removal of the proton between the carbonyls, they both become flat anionic molecules (Figure 2.6). 2-Methyl-1H-indene-1,3(2H)-dione (CO-9) is relatively easier to deprotonate and form the anionic species than cyclopent-4-ene-1,3-dione (CO-8) since control of removing the proton on the tertiary carbon of CO-9 can be easier than removing one of the protons on the secondary carbon of CO-8, which contains four protons in total.

\[
\text{Scheme 2.3. Reaction scheme for the synthesis of 2-methyl-1H-indene-1,3(2H)-dione (CO-9).}\textsuperscript{42c}
\]

The first question that must be asked is whether the bulkiness of the phenyl groups creates steric hindrance which might prevent formation of quasicrystals with 5*-\textsubscript{r}, 3*-\textsubscript{r}, and 2*-croconate tiles \textit{via} metal coordination in monolayers. Fortunately, this Penrose tiling system with croconate and its derivatives contains not only the gaps of star, crown and rhombus but also sufficient spaces available in the pentagons as shown in Figure 2.7. Croconate and its derivatives are linked vertex to vertex \textit{via} metal-carbonyl bonds. The position of the metal linkage is the centre of sides of the actual pentagon.
The second candidate in the monomeric molecules category is the cyano-substituted cyclopentadienyl which is an anionic molecule substituted with cyano linkers (Figure 2.8). Unlike carbonyl linkers that coordinate to a metal in bond angle of around 140°, the linear intermolecular linkage of cyanocyclopentadienyls between the tiles can be achieved by metal coordination. Metals that link can preferably form linear geometry with the cyano-substituents CN – M – NC are silver and copper. Sufficient space for counter ions will occur around the linkage as well as spaces in between the pentagons as shown in Figure 2.7. Alternatively, square-planar coordination geometry can also be possible if the other ligands are sufficiently small that CN – M – NC bonds are still linear as shown in Figure 2.8e. The syntheses of 5*--, 3*- and 2*-cyanosubstituted cyclopentadienyl ions have been reported and a recent publication describes an optimised synthetic procedure for the 5*-tile. Therefore, pentacyanocyclopentadienide anion (PCN-3) was prepared by following the optimised preparation (Scheme 2.4a).
Figure 2.8. a) 5*-., b) 3*-., c) 2*-cyanosubstituted cyclopentadienyl ions, d) linear-geometric coordination linkage of Ag⁺ with 5*- and 3*-cyanosubstituted cyclopentadienyl ions and e) another example of square-planer coordination geometry (M = metal, L = ligand).

2.1.2.1 Pentacyanocyclopentadienyl

Overall, two pathways to synthesise the pentacyanocyclopentadienyl anion have been reported. One is only a two-step reaction although sodium cyanide and carbon disulfide were used as shown in Scheme 2.4a. Sodium cyanide is a UN hazard class 6 (poison) chemical and the flash point of carbon disulfide is -43 °C which is highly flammable. The other method shown in Scheme 2.4b requires a lot of reaction steps and the final step utilises copper cyanide which is also UN hazard class 6.1 (poison) chemical. The overall yield for Scheme 2.4a is regarded to be higher than Scheme 2.4b. Therefore, Scheme 2.4a was selected to carry out for synthesis of pentacyanocyclopentadienyl tetraethyl ammonium (PCN-3).
Two different reaction schemes for the formation of the pentacyanocyclopentadienyl ion (PCN-3).\textsuperscript{55-56}

The intermediate product in Scheme 2.4a, 1,4-dithiine-2,3,5,6-tetracarbonitrile (PCN-2), was impure with a small amount of the by-product sulfur although most of sulfur was washed out with carbon disulfide using Soxhlet extraction technique for three days. This intermediate was recrystallised from toluene and became sufficiently pure for the further reaction. In the next step sodium pentacyanocyclopentadienide was formed in 7\% yield. Ion exchange to the bulkier tetraethyl ammonium cation gave a yellow precipitate which was then recrystallized from ethanol multiple times to produce a purer product.
2.1.2.2 Tri- and di-cyano cyclo pentadienyl: 3* and 2*

Webster has studied polycyanation on cyclopentadiene using cyanogen chloride and sodium hydride. The cyano-substituted products shown in Figure 2.9 a-h have been synthesised and successfully isolated. Mono-, di-, tri-, tetra- and penta-substitution were conducted separately and the crude products were purified by recrystallization, ion exchange and/or acidic alumina column chromatography. Figure 2.9b and Figure 2.9c are candidates for the 3* tile and Figure 2.9d for the 2* tile. The major drawback of those reactions is the use of cyanogen chloride which is highly toxic blood agent and UN hazard class 2.3. Due to toxicity of the reagent, these reactions were not carried out at this stage.

2.2 Macrocycles

2.2.1 Campestarene

Guieu and colleagues have synthesised 5-fold symmetric macrocycles structured with five phenols bridged by Schiff base imines. It was suggested that 3-centre hydrogen dictates the macrocycle geometry and the macrocycle core is stabilised by tautomerisation via the 3-centre hydrogen bonds between the internal OH and the imine nitrogen (Figure 2.10). According to ab initio DFT calculations reported by the authors, although the enol-imine and the keto-enamine forms of campestarenes are
Both flat and relatively low in energy in comparison with the corresponding hexamers, the most stable formation is the enol-imine form (Figure 2.10a left). Unfortunately, single crystal X-ray diffraction structures of any campestarenes have not yet been reported and all attempts to grow single crystals of campestarenes synthesised in this project have been unsuccessful.

Figure 2.10. a) The enol-imine form with a shared hydrogen bond (left), the zwitterionic structure (centre) and the keto-enamine form (right) of Cam-1. The major change of hydrogen bonding is highlighted in red. b) enol-imine tautomer (left) and keto-enamine tautomer (right) predicted by B3LYP/6-31G*. grey: C, red: O, blue: N, white: H (reproduced from ref. 34).

Alkyl- or linker-substituted phenols containing aldehyde and nitro group at both ortho-positions are the precursors for syntheses of campestarenes. The nitro group is reduced by sodium dithionite to form a primary amine which reacts with the aldehyde to afford oligomers and further completion of the cyclisation to yield campestarenes. Intermediate oligomers have not been isolated. This reaction was conducted in about 10% water in ethanol under reflux for two hours, although the colour change of the reaction mixture from orange to purple, which is a distinctive product colour, was observed within 5-20 minutes. The crude product was purified by neutral alumina column chromatography eluted with 10% methanol in dichloromethane. Because of the tailing behaviour of campestarene on neutral alumina by TLC, a large volume of the eluent was required to collect all of the synthesised product.
Penta-\textit{tert}-butyl-campestarene \textbf{Cam-1} has been reported\textsuperscript{34} and was synthesised here to understand the nature of campestarenes. In addition, the synthesised \textbf{Cam-1} can be used for deposition studies as a model tile. Reaction of 4-(\textit{tert}-butyl)phenol with paraformaldehyde gave the ortho-substituted aldehyde compound \textbf{C-1} which was nitrated using fuming HNO\textsubscript{3} to give the \textit{tert}-butyl containing precursor \textbf{C-2}. Using sodium dithionite as a reagent, the cyclisation was achieved to synthesise \textbf{Cam-1} in quantitative yield (Scheme 2.5). The \textsuperscript{1}H NMR spectrum of the synthesised \textbf{Cam-1} shows peaks for both monomer and dimer species (Figure 2.11). \textbf{Cam-1} aggregates as a dimer at ambient condition as reported in the literature.\textsuperscript{34}

\begin{center}
\textbf{Scheme 2.5. Example of reaction scheme for the synthesis of penta-\textit{tert}-butyl-campestarene (Cam-1).}\textsuperscript{34}
\end{center}

\begin{center}
\textbf{Figure 2.11.} \textsuperscript{1}H NMR spectrum of penta-\textit{tert}-butyl campestarene (Cam-1) in $d_6$-DMSO. \text{x} is impurity.
\end{center}
2.2.1.1 5*-Campestarenes

Two methods to attaching linkers on campestarenes designed for this project were pre- and post-synthesis derivatisation. Campestarene tiles are required to contain linkers (carboxylate, cyano and pyridyl groups) around their periphery. Substitution of the linkers onto campestarenes can be achieved before or after the cyclisation. Therefore, we explored the pre- and post-cyclisation derivatisation using protection-deprotection techniques and Suzuki cross coupling. The boronic acids used for Suzuki cross coupling were 4-boronobenzoic acid, pyridin-4-ylboronic acid and (4-cyanophenyl)boronic acid which were purchased. 4-borono-2-butylbenzoic acid (B-1) and 4-borono-2-heptylbenzoic acid (B-2) which were synthesised in this thesis were also used to improve the solubility of the resulting products.

2.2.1.1.1 Post-synthesis derivatisation of campestarenes

Post-synthesis derivatisation of campestarenes requires activation of the para-positions where a linker should be substituted and this can be achieved by removing a good leaving group such as bromide. In Scheme 2.6, using the bromine-containing precursor (C-3), pentabromo-campestarene (Cam-2) was synthesised and confirmed by NMR spectroscopy and MALDI-TOF mass spectrometry. Assignment of proton signals in Figure 2.12 was based on comparison of $^1$H NMR spectra of the other campestarenes synthesised in this project. The proton signals at 16.94 ppm, 9.21 ppm, 7.97 ppm and 7.53 ppm were assigned to OH, NCH and aromatic protons, respectively. The other signals at 14.72 ppm and 7.79 ppm could not be assigned. These unassignable peaks were consistently observed in $^1$H NMR spectra even after washing the crude product with dichloromethane, methanol and water for a few days using Soxhlet technique. The MALDI-TOF spectrum (Figure 2.13) shows peaks at 985.76 m/z for [M+H]$^+$, 1007.72 m/z for [M+Na]$^+$ and 1023.74 m/z for [M+K]$^+$ with the distinctive bromine isotope pattern. As expected, this purple product (Cam-2) was insoluble in most of common solvents. $^{13}$C NMR spectra of Cam-2 could not be obtained due to its poor solubility. Its poor solubility also influenced further reactions.
Scheme 2.6. Reaction scheme for post-synthesis derivatisation of campestarenes.

Figure 2.12. $^1$H NMR spectrum of Cam-2 in $d_6$-DMSO.
The addition of cyanide using copper cyanide in DMF was carried out with the crude pentabromo-campestarene (Cam-2) under reflux for a few days (Scheme 2.6). However, isolation of the product pentacyano-campestarene was unsuccessful as the solubility of pentacyano-campestarene is also predicted to be poor. The poor solubilities of both of the starting material and the product resulted in inconclusive results about whether the addition of cyano groups can be achieved by this route.

The other pathway to derivatisation of campestarene is Suzuki cross-coupling using substituted phenyl boronic acid catalysed with tetrakis(triphenylphosphine)palladium(0) (Scheme 2.6). This reaction has not been carried out due to poor solubility of the starting material (Cam-2). Moreover, campestarenes are unstable in strongly basic conditions such as aqueous 1 M NaOH. Loss of the internal -OH hydrogens in the core of campestarenes breaks the entire campestarene system, causes cleavage of the imine bridges and the macrocycle falls apart. This Suzuki cross-coupling requires a base, sodium carbonate, and heating above 100 °C. Under such reaction conditions and the problems with the starting material (Cam-2), Suzuki cross-coupling of campestarenes is not promising for the production of campesterene substituted with linkers.
Instead of direct functionalisation of the carbons at the para-positions, ether-type addition was also an alternative methodology for attaching linkers to campestarene (Scheme 2.7). Synthesis of pentamethoxy-campestarene (Cam-3) was carried out under almost the same reaction conditions for synthesis of penta-tert-butyl campestarene (Cam-1), except for the purification step. The crude Cam-3 was washed with dichloromethane, methanol and water using Soxhlet technique to yield a purple solid, instead of alumina column chromatography. As predicted, the solubility of pentamethoxy campestarene (Cam-3) was so poor that only DMSO and DMF are suitable solvents.
Pentamethoxy campestarene (Cam-3) was characterised by $^1$H NMR spectroscopy (Figure 2.14) and MALDI-TOF mass spectrometry (Figure 2.15). Due to its extremely poor solubility even in $d_6$-DMSO, $^{13}$C NMR and other 2D NMR spectra were unable to be obtained. Therefore, the proton peaks in $^1$H NMR spectrum of Cam-3 in $d_6$-DMSO could be assigned based on comparison of the published $^1$H NMR spectrum of Cam-1 in $d_6$-DMSO. As Cam-3 is a symmetric molecule, only five signals were observed. The five signals were all broad singlets and the broadening (no splitting) could be associated with the poor solubility of Cam-3. The signals for the internal OH and imine protons of Cam-3 were
assigned at 16.33 ppm and 9.29 ppm, respectively, compared to the internal OHs and imine protons of **Cam-1** which appear at 17.10 ppm and 9.45 ppm. The signals for the protons on aromatic rings of **Cam-3** were assigned at 7.55 ppm and 7.12 ppm (**Cam-1**: 8.03 ppm and 7.52 ppm). The only remaining signals at 3.84 ppm was assigned to the methoxy protons of **Cam-3**. The signals of OH, imine and aromatic protons of **Cam-3** all integrated as five protons each and the signal of the methoxy proton of **Cam-3** integrated as fifteen protons. It is interesting that $^1$H NMR spectrum for **Cam-1** shows peaks for both monomer and dimer of **Cam-1** whereas only one type of **Cam-3** was found in $^1$H NMR spectrum for **Cam-3** and it was most likely a monomer, according to MALDI-TOF analysis (Figure 2.15) where peaks at 746.3896 m/z for [M+H]$^+$, 768.3630 m/z for [M+Na]$^+$, 784.3323 m/z for [M+K]$^+$, 823.4519 m/z for [M+2K-H]$^+$, 845.0015 m/z for [M+2K+Na-2H]$^+$ and 860.9521 m/z for [M+3K-2H]$^+$ were observed. Figure 2.11 shows that **Cam-1** tends to aggregate as a dimer at room temperature since the peaks for both monomer and dimer were observed.$^{34}$

The next step, de-methylation using boron tribromide, was carried out under reflux. Although **Cam-3** was insoluble in dichloromethane, often reactions occur on the surface of undissolved starting materials and de-methylation was expected to occur on the surface of **Cam-3** and partial de-methylation was observed in $^1$H NMR spectra (Figure 2.16). De-methylation of **Cam-3** was attempted twice, using 5 and using 15 equivalents of BBr$_3$ to **Cam-3**. After cooling to r. t., the reaction mixtures with suspension of the purple solid was quenched with water. The purple solid was collected by filtration and washed with methanol using the Soxhlet technique.
In Figure 2.16 all the peaks for the demethylated Cam-3 were shifted slightly upfield except for the methoxy proton. Another imine proton peak was observed. Obviously, the intensity of the methoxy proton peak decreased significantly but the methoxy proton peak did not completely disappear. All the peaks for OH, imine, aromatic and methoxy protons, including the additional imine proton peak, integrated almost the same. The very similar \(^1\)H NMR spectra of the de-methylated Cam-3 using either 5 or 15 equivalents of BBr\(_3\) to Cam-3 indicate that excessive amount of the de-methylation reagent did not complete the de-methylation. NOESY spectra of both of the de-methylated Cam-3 samples were obtained to assign the two imine peaks. NOE correlations between imine and aromatic protons were the same in both of the NOESY spectra. As shown in Figure 2.17, NOE correlation for the two imine proton peaks to the aromatic protons were observed. However, it is still ambiguous that, as highlighted in the green line, NOE correlation for the imine proton peak at 9.2 ppm to the aromatic protons was found only in the vertical line, not in the horizontal line whereas NOE correlation for the imine proton peak at 9.1 ppm to the aromatic protons was found in both vertical and horizontal lines. Poor solubility of the product even in \(d_6\)-DMSO prevented obtaining \(^{13}\)C and related 2D NMR spectra. Moreover, due to broadening of the peaks in \(^1\)H NMR spectra (Figure 2.16), it was hard to anticipate the structure and symmetry of the product based on peak-splittings as well as purity of the product between homogeneous partially de-methylated campestarenes and a mixture of hydroxy-campestarenes containing different number of remaining methoxy groups. To test the feasibility of
addition onto hydroxyl-campestarene several attempts to attach carboxylates onto the para-OH of the hydroxy-campestarenes containing some methoxy groups were unsuccessful. Therefore, this ether-type addition method was discontinued in this project.

Figure 2.17. NOESY spectrum of de-methylated Cam-3 using 5 equivalents of BBr₃ to Cam-3. NOE correlation between imine and aromatic protons highlighted in the green line for the peak at 9.2 ppm and in red line for the peak at 9.1 ppm.

2.2.1.1.2 Pre-synthesis derivatisation of campestarenes

The other pathway, pre-synthesis derivatisation followed by cyclisation, has successfully led to production of campestarenes substituted with proper linkers. Scheme 2.8 shows mono-substitution of phenol, hydroquinone or the mono-protected hydroquinone with ester to synthesise ester-substituted phenols (C-9, C-10 and C-11). Protection and de-protection with sulfonate (C-6) and benzyl groups (C-7 and C-8) led to mono-substituted hydroxybenzene with ethyl ester (C-9 and C-11) which can be a carboxylic acid linker after de-esterification. The other one step mono-substitution of hydroquinone with tert-butyl ester was successful to synthesise C-10 whereas one step mono-substitution of hydroquinone with ethyl ester using ethyl bromoacetate or ethyl bromopropionate as a reagent was attempted several times under various conditions and the collected products were the unreacted hydroquinone and/or the bi-substituted compound. It was surprising that the size of alkyl ester played a significant role on mono- or bi-substitution of hydroquinone. In addition, among the three methods to synthesise mono-substituted phenols with ester, the benzyl protection and de-protection method (via C-7 and C-8) was best in terms of product yield and scale-up feasibility.
Next, sequential ortho-directed addition of the aldehyde to form C-12, C-13 and C-14, followed by a nitro group yielded the ester precursors (C-15, C-16 and C-17) which were then cyclised to form the penta-ester campestarene (Cam-4). From the cyclisation using C-17 as a precursor flash alumina column chromatography using 4% methanol in dichloromethane as eluent purified the purple product Cam-4. However, several de-esterification attempts of penta-ethyl ester campestarene (Cam-4) to synthesise Cam-6 were all unsuccessful. Campestarenes are unstable in strong acidic/basic media which is a requirement for de-esterification. If acidity/basicity is too low, the hydrolysis of the ester does not occur even with heating and if the acidity/basicity is too high, campestarenes decompose. Therefore, prior to cyclisation, the ester monomers, C-15, C-16 and C-17, were de-esterified to form carboxylic acids (C-18 and C-19) which were then cyclised to give carboxylic-substituted campestarenes, Cam-5 and Cam-6. Cyclisations using the ester precursors, C-15 and C-16, were not carried out.

Cam-4, Cam-5 and Cam-6 were characterised by $^1$H NMR spectroscopy (Figure 2.18). Due to its extremely poor solubility even in $d_6$-DMSO, $^{13}$C NMR and other 2D NMR spectra were unable to be obtained. Therefore, the proton peaks in $^1$H NMR spectrum of Cam-4, Cam-5 and Cam-6 in $d_6$-DMSO could be assigned based on comparison of the published $^1$H NMR spectrum of Cam-1$^{34}$ and Cam-3 in $d_6$-DMSO as well as their monomer precursors, C-17, C-18 and C-19. As Cam-4, Cam-5 and Cam-6 are symmetric molecules, only 8, 5 and 6 signals for Cam-4, Cam-5 and Cam-6 were observed, respectively. All the signals were all broad singlets and the broadening (no splitting) could be associated with the poor solubility of these campestarenes. The signals for the internal OH of Cam-4, Cam-5 and Cam-6 were assigned at 16.51 ppm, 16.39 ppm and 16.49 ppm, respectively, compared to the internal OHs of Cam-1 and Cam-3 which appear at 17.10 ppm and 16.34 ppm. The signals for the imine protons of Cam-4, Cam-5 and Cam-6 were assigned at 9.27 ppm, 9.31 ppm and 9.30 ppm, respectively, compared to the imine protons of Cam-1 and Cam-3 which appear at 9.45 ppm and 9.26 ppm. The signals for the protons on aromatic rings of Cam-4 were assigned at 7.67 ppm and 7.06 ppm, those of Cam-5 were assigned at 7.66 ppm and 7.12 ppm and those of Cam-6 were assigned at 7.66 ppm and 7.06 ppm (Cam-1: 8.03 ppm and 7.52 ppm and Cam-3: 7.53 ppm and 7.51 ppm). For Cam-4 the aliphatic signals at 5.01 ppm, 4.22 ppm, 1.57 ppm and 1.23 ppm were assigned to H1, H3, H2 and H4, respectively in comaparison with the ethyl ester protons of the precursor, C-17 which appear at 4.79 ppm, 4.27 ppm, 1.66 ppm and 1.30 ppm. In COSY spectroscopy of Cam-4 correlations between H1 and H2 as well as between H3 and H4 were observed. For Cam-5 the remaining signal at 4.75 ppm was assigned to the methylene protons which was consistent with the corresponding protons
on the precursor, C-18 at 4.76 ppm. For Cam-6 the remaining signals at 4.90 ppm and 1.57 ppm were assigned to H1 and H2, respectively, compared to the corresponding protons on the precursor, C-19 which appear at 4.85 ppm and 1.70 ppm. The signals of OH, imine and aromatic protons of Cam-4, Cam-5 and Cam-6 all integrated as five protons each. The signals of H1, H3, H2 and H4 of Cam-4 integrated as 5, 10, 15 and 15 protons, respectively. The signal of the methylene protons of Cam-5 integrated as 10 protons. The signals of H1 and H2 of Cam-6 integrated as 5 and 15 protons, respectively. Consistent with observation in 1H NMR spectrum for Cam-3 where only one type of Cam-3 was found and it was most likely a monomer, the corresponding dimer species were not observed in 1H NMR spectra of Cam-4, Cam-5 and Cam-6.
Scheme 2.8. Reaction scheme for the synthesis of penta-ethyl propionate (Cam-4), penta-acetoxy campestarenes (Cam-5) and penta-propionoxy (Cam-6). R₁ = H or CH₃, R₂ = Et or t-butyl.
These penta-acet/propionoxy campestarenes (Cam-5 and Cam-6) are distinctive dark purple solids which can be the 5* tiles. For purification of these campestarenes neutral alumina column chromatography eluted with about 10% methanol in dichloromethane (used for Cam-1) was inapplicable to such highly polar macrocycles. After flash silica or alumina column chromatography of those campestarenes, in the $^1$H NMR spectrum (Figure 2.19) peaks for the 3-centre hydrogens which usually appear between 15 and 20 ppm (highlighted in the red box) and for the imine bridges which usually appear between 9 and 10 ppm (highlighted in the yellow box) disappeared although the colour of the collected fraction remained purple.
Successful purification of the carboxylate campestarenes was achieved using Sephadex G-10 column chromatography followed by acid-base washing. Without the Sephadex G-10 column chromatography, acid-base washing can successfully remove most of by-products and other organic/inorganic impurities. However, some peaks that cannot be assigned were still present as shown in Figure 2.20 which proves that Sephadex G-10 column chromatography is required for completion of purification of carboxylate-substituted campestarenes. Sephadex G-10 column chromatography is usually used to separate large organic molecules such as macrocycles and peptides from small inorganic salts. The purified product was confirmed by MALDI-TOF mass spectrometry where the Cam-5 peaks at 964.27 m/z for [M-H]', 986.26 m/z for [M+Na-2H]' and 1002.26 m/z for [M+K-2H]' (Figure 2.21) and the Cam-6 peaks at 1036.28 m/z for [M+H]', 1058.25 m/z for [M+Na]' and 1074.23 m/z for [M+K]' (Figure 2.22) were observed.
Figure 2.21. MALDI-TOF spectrum of **Cam-5**.

Figure 2.22. MALDI-TOF spectrum of **Cam-6**.
Those two carboxylate-containing 5* tiles have some drawbacks. Firstly, Cam-5 is insoluble in most of common organic solvents whereas Cam-6 can be dissolved in methanol. For liquid phase deposition 5*- , 3*- and 2*-tiles with 5-fold symmetry have to be fully dissolved in common organic solvents in order for those tiles to self-assemble in such quasicrystalline ordering. Non-volatile solvents such as water, DMSO and DMF cannot be used. In particular, water creates a ‘coffee ring effect’ during evaporation and instead of forming monolayers, molecules tend to aggregate at the edges of the ‘coffee rings’. Thus, for liquid phase deposition a mixture of basic aqueous solution and methanol might be the only option to avoid the coffee ring effect as well as to fully dissolve the carboxylate-containing campestarenes.

Another concern is purity of Cam-6 that contains chiral centres on the five propionic acid groups as shown in red circles in Figure 2.23. Since the precursor, C-19, is a mixture of stereoisomers, the campestarene must be a mixture of eight enantiomers. Cam-6 is a mixture of stereoisomers but it is pure once other organic and inorganic impurities have been removed. Moreover, the chiral centres are sufficiently far apart to not create any noticeable chemical shift or splitting of peaks in the \( ^1 \text{H} \) NMR spectrum of Cam-6.
Figure 2.23. Structures of Cam-6 (top right) and its precursor C-19 (top left). Chiral centres (*) are highlighted in red circles. Simplified eight stereoisomers of Cam-6 (bottom).

Another technique to attach linkers onto tiles is Suzuki cross-coupling using boronic acids substituted with linkers such as phenyl-carboxylic acid, cyano-phenyl and pyridyl (Scheme 2.9). 4-Boronobenzoic acid, (4-cyanophenyl)boronic acid and pyridin-4-ylboronic acid are commercially available. Precursor C-3 was reacted with these boronic acids under basic conditions catalysed by tetrakis(triphenylphosphine)palladium(0), with heating at 105 °C for 5 hours to yield the biphenyl-type monomer precursors (C-20, C-21 and C-22) as orange solids. These were then cyclised to form penta-benzoic acid campestatene (Cam-7), penta-cyanophenyl campestatene (Cam-8) and penta-pyridinyl campestatene (Cam-9) as crude products, respectively.
Scheme 2.9. Reaction scheme for the syntheses of penta-benzoic acid campestarene (Cam-7), penta-cyanophenyl campestarene (Cam-8) and penta-pyridyl campestarene (Cam-9).

This biphenyl system rendered the solubility of Cam-7, Cam-8 and Cam-9 even poorer and therefore the Soxhlet washing technique was used to purify the crude products of Cam-7, Cam-8 and Cam-9 with dichloromethane, methanol and water to give a purple solid. Although MALDI-TOF mass spectrometry detected peaks for \([\text{M+H}]^+\), \([\text{M+Na}]^+\) and \([\text{M+K}]^+\) of Cam-7, Cam-8 and Cam-9, \(^1\text{H}\) and related 2D NMR spectroscopy could not confirm that Cam-7, Cam-8 and Cam-9 have been synthesised and purified successfully. In particular, \(^1\text{H}\) NMR spectra of Cam-7, Cam-8 and Cam-9 (Figure 2.24) always showed exceptionally broad peaks at around 7 – 8 ppm where the aromatic peaks for campestarenes usually appear as well as unidentifiable peaks as shown in Figure 2.24a. Consistent observation of those broad peaks could indicate that organic and inorganic impurities were still present after the Soxhlet washing purification method and those impurities could account for those unidentifiable peaks at around 7.5 ppm and 5 ppm. Otherwise, \(\pi-\pi\) stacking of the biphenyls of those campestarenes resulted in aggregation which generated campestarene polymers. Even after the Soxhlet washing for 15 days to eliminate possibility of presence of impurities, broad peak and unassignable peaks at around 7.5 ppm were still present although a sharp peak for distinctive 3-centre internal hydrogen was observed at 19.23 ppm, as shown in Figure 2.24b.
Solubility of \textbf{Cam-7}, \textbf{Cam-8} and \textbf{Cam-9} was the major obstacle. In order to increase the solubility of those biphenyl campestarenes, an alkyl chain was attached onto the precursors at the \textit{meta}-position. The benzoic acid precursors, \textbf{C-23} and \textbf{C-24}, were successfully synthesised, purified and fully characterised by 1D and 2D NMR spectroscopy and ESI mass spectrometry. The cyanophenyl precursor, \textbf{C-25}, which was synthesised and confirmed by ESI mass spectrometry has been purified several times by silica column chromatography but still impure with by-products. Optimisation of eluent system for \textbf{C-25} is required.
Scheme 2.10. Reaction scheme for the syntheses of penta-benzoic acid campestarene (Cam-10), penta-cyanophenyl campestarene (Cam-11) and penta-pyridinyl campestarene (Cam-12).

Syntheses of penta-benzoic acid campestarenes (Cam-10 and Cam-11) were successfully achieved (Scheme 2.10) and the campestarene products were confirmed by MALDI-TOF mass spectrometry where [M+H]+, [M+Na]+ and [M+K]+ peaks were observed. The alkyl chains certainly improved solubility of the crude products which could be dissolved in methanol. Moreover, the crude product of the \( n \)-heptyl chain substituted campestarene (Cam-11) was even soluble in dichloromethane. Purification for the other penta-carboxylic acid campestarenes (Cam-5 and Cam-6), was achieved by Sephadex G-10 column chromatography, followed by acid-base washing using 0.1 M hydrochloric acid and 0.1 M sodium hydroxide solutions, was applied to the crude products of Cam-10 and Cam-11. During this purification process, organic and inorganic impurities were removed as expected. As shown in Figure 2.25a and Figure 2.25c, peaks of organic impurities disappeared in the \( ^1 \)H NMR spectra of both Cam-10 and Cam-11 after the purification in comparison with \( ^1 \)H NMR spectra of their crude products. However, the peak broadening which was problematic in \( ^1 \)H NMR spectra of the biphenylcampestarenes without alkyl chains (Cam-7, Cam-8 and Cam-9) was still observed in the \( ^1 \)H NMR spectra of both Cam-10 and Cam-11 (Figure 2.25). This peak-broadening is consistently observed in all of the \( ^1 \)H NMR spectra of the biphenyl-type campestarenes. This could be associated with aggregation by \( \pi-\pi \) stacking rather than the presence of impurities. More importantly, peaks for the 3-centre internal hydrogens that are usually observed between 16 – 20 ppm were not found in Figure 2.25a - d. After the purification of acid-base washing and Sephadex G-10 column
chromatography, solubility of **Cam-10** and **Cam-11** changed significantly. They both are partially soluble in methanol and any other common organic solvents cannot dissolve them apart from DMSO.

Figure 2.25. $^1$H NMR spectra in $d_6$-DMSO of a) **Cam-11**, b) crude **Cam-11**, c) **Cam-10** and d) crude **Cam-10**.

Another concern about biphenylcampestarenes containing carboxylic acids (**Cam-7**, **Cam-10** and **Cam-11**) could be unwanted intermolecular hydrogen bonding between the C-H hydrogen adjacent to the carboxylic acid on the phenyls and the oxygen on carboxylic acid as shown in Figure 2.26a. This type of intermolecular hydrogen bonding was reported by Alex Kandel for ferrocenecarboxylic acid deposited on Au(111). The intermolecular hydrogen bonding between carboxylic acid and hydrogen adjacent to carboxylic acid on ferrocene generated flower-like patterns with 5-fold symmetry. However, the oxygen on the carboxylic acid cannot approach to the hydrogen adjacent to the carboxylic acid on the phenyls close enough to form hydrogen bonding due to steric hindrance. Only intermolecular hydrogen bonding between carboxylic acids would be possible. In addition to steric hindrance, alkyl substitution on the meta-position of the phenyls also prevents the Figure 2.26a type hydrogen bonding.
a) Proposed geometry of intermolecular hydrogen bonding and b) corresponding geometry with Cam-7, Cam-10 and C-11 (R= H, n-C_4H_9, n-C_7H_15, respectively).

2.2.1.2 3*- and 2*-campestarenes

Scheme 2.11. Reaction scheme for the syntheses of 3*-campestarene (Cam-13) and 2*-campestarene (Cam-14).

The 3*- and 2*-campestarenes were synthesised using a 1:1 mixture of the tert-butyl (C-2) and the propionic acid (C-19) precursors under the same condition of 6 equivalents of sodium dithionite to the combined precursors in 10% water in ethanol under reflux for 2-3 hours (Scheme 2.11). As anticipated, not only the 3*- and 2*-campestarenes, but also 3*- and 2*-isomers as well as 1*, 4*- campestarene isomers and Cam-1 must have been produced (Figure 2.27). An appropriate characterisation technique
to differentiate 3*- and 2*-isomers from 3*- and 2*-campestarenes (Cam-13 and Cam-14) is different from characterisations for 1* and 4*-campestarenes. Characterisations of these campestarenes and isomers should be challenging. Based on the MALDI-TOF analysis (Figure 2.28), the presence of 4*-,, 3*-,, 2*-,, 1* and Cam-1 was confirmed. The purification method, acid-base washing using 0.1 M hydrochloric acid and 0.1 M sodium hydroxide solutions, followed by Sephadex G-10 column chromatography, could remove Cam-1. However, isolation and/or extraction of Cam-13 and Cam-14 from the mixture has not yet been successful since flash silica or alumina column chromatography that decomposed the 5*-campestarenes (Cam-5 and Cam-6) cannot be applied due to the high polarity of the products (Cam-13 and Cam-14). In addition, C-19 contains a chiral centre which again generated racemic mixtures of Cam-13 and Cam-14. By using the acetic acid precursor (C-18) the production of racemic mixtures can be avoided. Despite difficulties in isolation of the target products (Cam-13 and Cam-14), it will be still interesting to test the orientation of the isomer mixture with the 5*-campestarene (Cam-6) on a surface.

Figure 2.27. Structures of 3*-isomer, 2*-isomer, 4*-campestarene, 1*-campestarene and Cam-1.
Figure 2.28. MALDI-TOF spectrum of the mixture of isomers containing 3*- and 2*-campestarenes. 0*= Cam-1, 1*= 1*-campestarene, 2*= Cam-14 or 2*-isomer, 3*= Cam-13 or 3*-isomer, 4*= 4*-isomer.
2.2.2 Singapore Pentamers, SP

Since Huaqiang Zeng and co-workers from National University of Singapore synthesised the circular aromatic pentamer (SP-1) by a chain-extension method followed by cyclisation in 2008 (Scheme 2.12), his group developed a synthetic methodology based on a one-pot synthesis and explored other circular aromatic pentamers by introducing diverse functionalities at selected positions, replacement of the internal methoxy groups with fluoride and use of pyridone as a base building-block instead of phenyl. His group has also reported intensive studies on the circular aromatic pentamer (SP-1) such as cation binding to the methoxy core, de-methylation and optimisation of the one-pot synthesis. Due to no officially reported name for those pentamers synthesised by Huaqiang Zeng’s group, in this thesis Huaqiang Zeng’s pentamers are named Singapore Pentamers (SP).
Figure 2.29. Structures of methoxyphenyl- (left), fluorophenyl- (middle) and pyridone-based (right) Singapore Pentamers.\textsuperscript{35, 57-63}

Methoxy SPs (SP-1, SP-2, SP-3, SP-4 and SP-5) are a spinning top-like shape where two non-adjacent methyls of the five internal methoxy groups are up and the other three methyls are down from the relatively flat bodies to minimise the steric hindrance as shown in Figure 2.30. Slight distortion of the main bodies is observed due to the methoxy methyls which could still be slightly sterically hindered to each other. 3-Centre hydrogen bonding between the amide proton and the two adjacent oxygens on the methoxy in the core was observed in X-ray crystallography and DFT calculations of SP-1, SP-2 and SP-3. Although methoxy SPs are not completely flat, Huaqiang Zeng’s group has studied the synthetic methodologies including selective functionalization around the periphery of methoxy SPs as well as their isolation and characterisation. Furthermore, fluoro-Singapore Pentamer (SP-7) is a relatively new pentamer which is completely flat although functionalization of fluoro-SPs and one-pot synthesis for SP-7 have not yet been reported (Figure 2.29). The advantage of SP-7 is that only 2 steps will be required to synthesise SP-7 if the one-pot synthesis for SP-7 can be achieved. One-pot synthesis of SP-7 will be described in this thesis. 3-Centre hydrogen bonding between the amide proton and the two adjacent fluorines in the core was observed in X-ray crystallography and DFT calculation of SP-7.\textsuperscript{59}
Figure 2.30. Crystal structure of SP-1 generated by Mercury (3.5.1) in Ball and Stick representation: top view (left) and side view (right) both with methoxy methyl groups in spacefill representation.\textsuperscript{35}

Pyridone-based SPs\textsuperscript{60a} are not studied in this thesis for the following reasons. They have poor solubility in common organic solvents. Even the solubility of iso-butyl pyridone-based SP is so poor that simple washing with dichloromethane and methanol can purify the product. This implies that the pyridone-based SP without any functionality must be incredibly insoluble and substitution with linkers might be difficult. One-pot syntheses for the pyridone-based SPs are also low-yielding and the monomer precursors for the corresponding pyridone-based SPs are often insoluble in dichloromethane which is the best solvent for the one-pot synthesis of pyridone-based SPs. The alternative chain-extension method which is overall 1 – 2 % yielding with multiple steps is not practical. Moreover, their selective functionalization has not yet been reported.

\subsection*{2.2.2.1 5*-Singapore Pentamers}

Like the campestarenes (Scheme 2.6 - Scheme 2.9), pre- and post-cyclisation derivatisation needs to be considered. By analysing the cyclisation step where condensation occurs between the amine and carboxylic acid to couple the two monomers, extra reactive functionalities (linkers) on the monomer precursors should be protected or absent. Protection of linkers is also undesirable since multiple steps, including protection of carboxylic acid were required to synthesise the amine-carboxylic acid-containing precursors (S-17, S-18, S-19 and S-20). Protecting groups may not survive during those multiple steps or selective protection for the linker only might be challenging. Therefore, post-cyclisation derivatisation was pursued (Scheme 2.13).
Scheme 2.13. Reaction scheme for the synthesis of SP-6.
* denotes compounds prepared in this thesis.
Several attempts to brominate the para-positions of SP-1 using bromine or N-bromosuccinimide under various conditions were carried out but were unsuccessful. No brominated species were observed and/or isolated. Another concern about the bromination was that there are no means of perfectly controlled bromination at the target positions or isolation of the target product from a mixture of isomers. Bromination in the meta-position can occur after completion of para-bromination. Therefore, functionalization of SP-1 was discontinued and attempts to functionalise SP-2 and SP-3 were carried out.

SP-2, which has a better leaving group (methyl) than SP-3 (octyl), was selected for further reactions. In analysis of SP-2 the two types of methoxy groups, inner and outer are present. The inner methoxy groups are not as reactive as a typical methoxy group on a monomer, based on the literature. The maximum number of those inner methoxy methyls that can be removed is two. Two non-neighbouring methyl groups of SP-1 can be removed by 3 M hydrochloric acid in N-methyl-2-pyrrolidone, BBr$_3$ in dichloromethane or tetrabutylammonium bromide/chloride in THF. In this project, removal of the inner methyls is beneficial because the steric hindrance associated with the inner methyl groups can be reduced and the base of the methoxy SPs can become flatter. The drawback of removal of one or two inner methyls could be isolation of the isomers variably containing 3, 4 or 5 inner methyl groups. In contrast to the inner methyls, the outer methyls were expected to be more labile and common de-methylation reagents could achieve the completion of synthesis of the target compound.

Boron tribromide (BBr$_3$) was used as a de-methylation reagent to synthesise SP-5* from SP-2. Since any ether-type solvents such as diethyl ether and THF can react with BBr$_3$ and the ether can be cleaved, dichloromethane was used as a solvent. Ten equivalents of BBr$_3$ to SP-2 were added to a solution of SP-2 in dry dichloromethane and the reaction mixture was refluxed overnight. In Figure 2.31b integrations of the peaks for both sets of methoxy protons to those major peaks at 11.47 ppm, 9.83 ppm, 8.23 ppm and 7.14 ppm were definitely less than they were meant to be although all the major peaks could not be assigned. The peak assignment for the crude product in Figure 2.31b was anticipated based on Figure 2.31a and a NOESY NMR spectrum for the crude product where NOE correlation between the methoxy proton peaks at 3.94 ppm and amide proton peaks at around 11 ppm was observed but no correlation for the peaks at around 9 ppm. Moreover, the crude product was still acidic as a downfield shift of water peak at 4.62 ppm was observed.
In order to push the de-methylation to completion, 20 equivalents of BBr$_3$ were used. After overnight reflux, a small batch of the reaction mixture was taken out and the solid suspension was collected by filtration, washed thoroughly with water and dried under vacuum to give an off-white solid. It was promising that the $^1$H NMR spectrum of the crude product (Figure 2.32b) shows a slight decrease in integration of the methoxy peaks labelled 3 and 4. Another unassignable peak at 9.5 ppm, which could be internal or external OH peaks, was also observed. The reaction mixture was refluxed for another 24 hours and the resulting $^1$H NMR spectrum was identical to Figure 2.32b. Hence, another 20 equivalents of BBr$_3$ was added to the reaction mixture which was then refluxed for another 24 hours. After the work-up described above, its $^1$H NMR spectrum (Figure 2.32c) was obtained. Unfortunately, the resulting $^1$H NMR spectrum (Figure 2.32c) was almost identical to the previous spectrum (Figure 2.32b) in that peaks for the methoxy protons were still present and their integration showed no significant changes. Surprisingly, a decrease in intensity of peaks for the internal methoxy protons labelled 3 more than the outer methoxy protons labelled 4. In addition, intensities of tiny peaks near the major peaks increased significantly. ESI mass spectrometry of the reaction mixture of the 40 equivalents of BBr$_3$ to SP-2 (Figure 2.33) found that peaks for [SP-2-3CH$_3$+2H$^-$] at 852.2315 m/z, [SP-2-4CH$_3$+3H$^-$] at 838.2168 m/z, [SP-2-5CH$_3$+4H$^-$] at 824.2019 m/z, [SP-2-6CH$_3$+5H$^-$] at 810.1882 m/z, [SP-2-
7CH\textsubscript{3}+6H\textsuperscript{+}\at 796.1727 \text{m/z}, [\text{SP-2-8CH}_{3}+7H\textsuperscript{+}] at 782.1576 \text{m/z}, [\text{SP-2-9CH}_{3}+8H\textsuperscript{+}] at 768.1431 \text{m/z} and [\text{SP-2-10CH}_{3}+9H\textsuperscript{+}] at 754.1273 \text{m/z} in negative ionisation as well as [\text{SP-2-2CH}_{3}+2H+\text{Na}\textsuperscript{+}] at 900.1276 \text{m/z}, [\text{SP-2-3CH}_{3}+3H+\text{Na}\textsuperscript{+}] at 886.1149 \text{m/z}, [\text{SP-2-4CH}_{3}+4H+\text{Na}\textsuperscript{+}] at 872.1065 \text{m/z}, [\text{SP-2-5CH}_{3}+5H+\text{Na}\textsuperscript{+}] at 848.1926 \text{m/z}, [\text{SP-2-6CH}_{3}+6H+\text{Na}\textsuperscript{+}] at 834.1808 \text{m/z}, [\text{SP-2-7CH}_{3}+7H+\text{Na}\textsuperscript{+}] at 820.1675 \text{m/z}, [\text{SP-2-8CH}_{3}+8H+\text{Na}\textsuperscript{+}] at 806.1533 \text{m/z}, [\text{SP-2-9CH}_{3}+9H+\text{Na}\textsuperscript{+}] at 792.1380 \text{m/z} and [\text{SP-2-10CH}_{3}+10H+\text{Na}\textsuperscript{+}] at 778.1235 \text{m/z} in positive ionisation (Table 2.1). This ESI-MS confirmed that \text{SP-2} had lost only two methyl groups. The result of NMR spectroscopy and ESI mass spectrometry analyses concludes that inertness of SPs was much higher than that was anticipated and thus a better leaving group than methyl needs to be used in SPs.

Table 2.1. Formulas and mass values for the reaction mixture of the 40 equivalents of BBr\textsubscript{3} to \text{SP-2} found in ESI-MS.

<table>
<thead>
<tr>
<th>Positive ionisation</th>
<th>Negative ionisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>Mass (m/z)</td>
</tr>
<tr>
<td>[\text{SP-2-2CH}_{3}+2H+\text{Na}\textsuperscript{+}]</td>
<td>900.1276</td>
</tr>
<tr>
<td>[\text{SP-2-3CH}_{3}+3H+\text{Na}\textsuperscript{+}]</td>
<td>886.1149</td>
</tr>
<tr>
<td>[\text{SP-2-4CH}_{3}+4H+\text{Na}\textsuperscript{+}]</td>
<td>872.1065</td>
</tr>
<tr>
<td>[\text{SP-2-5CH}_{3}+5H+\text{Na}\textsuperscript{+}]</td>
<td>848.1926</td>
</tr>
<tr>
<td>[\text{SP-2-6CH}_{3}+6H+\text{Na}\textsuperscript{+}]</td>
<td>834.1808</td>
</tr>
<tr>
<td>[\text{SP-2-7CH}_{3}+7H+\text{Na}\textsuperscript{+}]</td>
<td>820.1675</td>
</tr>
<tr>
<td>[\text{SP-2-8CH}_{3}+8H+\text{Na}\textsuperscript{+}]</td>
<td>806.1533</td>
</tr>
<tr>
<td>[\text{SP-2-9CH}_{3}+9H+\text{Na}\textsuperscript{+}]</td>
<td>792.1380</td>
</tr>
<tr>
<td>[\text{SP-2-10CH}_{3}+10H+\text{Na}\textsuperscript{+}]</td>
<td>778.1235</td>
</tr>
</tbody>
</table>
Figure 2.33. ESI-MS spectra of de-methylated SP-2 using 40 equivalents of BBr₃ to SP-2 in negative (top) and positive ionisation (bottom).

The selected better leaving group and O-protecting group for this methoxy-SP system was the benzyl group. The reaction conditions for the benzyl-containing monomers up to S-16* were the same as for the other methoxy- and octyloxy-containing intermediates. The last step to synthesise the monomer
precursor (S-20*) was reduction of the nitro group to the amine by hydrogenation using a metal catalyst. Palladium on carbon was used for syntheses of the other monomers (S-17, S-18 and S-19) and the reduction was carried out at 40 °C under H₂ pressure of 450 kPa for 17 – 18 hours since the reductions for S-17, S-18, and S-19 did not occur under mild conditions (room temperature and/or ambient pressure). When the reduction of the benzyl-containing monomer (S-16*) was carried out under the same conditions (palladium on carbon at 40 °C under H₂ pressure of 450 kPa for 17 – 18 hours) to yield the amine-benzyl-containing monomer (S-20*), both nitro reduction and de-protection of the benzyl group occurred simultaneously to yield S-21* instead of S-20*. In order to avoid the loss of the benzyl group during the reduction of the nitro group it was essential that the mild reduction conditions were used but a more reactive catalyst than palladium on carbon was also required. Therefore, the catalyst was replaced with platinum on carbon which is more reactive and often used to reduce nitro groups to amines. The reduction of S-16* was carried out using platinum on carbon as a catalyst at room temperature under H₂ atmosphere at balloon pressure for 12 hours and S-20* was successfully produced. (Scheme 2.14)

![Scheme 2.14. Reaction scheme for the syntheses of S-20* and S-21*](image)

The benzyl ether S-20* and the hydroxyl compound S-21* were characterised by NMR spectroscopy (Figure 2.34 and Figure 2.35) and ESI mass spectrometry. In the ^1H and ^13C NMR spectra of S-20* the presence of the peaks for the methylene and aromatic protons and carbons of the benzyl group were
a clear indication that the O-protecting benzyl was still attached to the oxygen of the monomer, in comparison with $^1$H and $^{13}$C NMR spectra of S-21* where the peaks for the methylene and aromatic protons and carbons of the benzyl group disappeared. The presence of the benzyl on the monomer (S-20*) was also in agreement with the ESI mass spectrum of S-20* where 274.1068 m/z for [M+H]$^+$ and 296.0885 m/z for [M+Na]$^+$ were found, whereas 206.0428 m/z for [M+Na]$^+$ was found in the ESI mass spectrometry spectrum of S-21*. Success of the reduction of the nitro group could also be confirmed by the obvious peak shifting observed in the $^1$H and $^{13}$C NMR spectra of S-20*, compared to those spectra of S-16* (Figure 2.36). The peaks for the aromatic protons were shifted upfield due to replacement of a strong electron-withdrawing group (nitro) with electron-donating group (amine). Moreover, significant upfield shift of peaks for the aromatic carbons labelled 2, 3, 4, 5 and 6 were observed in Figure 2.37.

Figure 2.34. $^1$H NMR spectra of S-20* (top) in CDCl$_3$ and S-21* (bottom) in d$_6$-DMSO.
Figure 2.35. $^{13}$C NMR spectra of S-20* (top) in CDCl$_3$ and S-21* (bottom) in $d_6$-DMSO.

Figure 2.36. $^1$H NMR spectra in CDCl$_3$ of S-16* (top) and S-20* (bottom).
Using this monomer (S-20\textsuperscript{*}) benzylxy SP (SP-4\textsuperscript{*}) was synthesised and characterised by NMR spectroscopy and ESI mass spectrometry, whereas attempts to cyclise the hydroxy monomer (S-21\textsuperscript{*}) to directly produce the hydroxy SP (SP-5\textsuperscript{*}) were unsuccessful. An assignment of \textsuperscript{1}H and \textsuperscript{13}C NMR spectra of SP-4\textsuperscript{*} (Figure 2.38) was possible with the aid of COSY, HSQC and HMBC experiments (Figure 2.39 – Figure 2.41). SP-4\textsuperscript{*} was symmetric since only eight sets of signals were observed in \textsuperscript{1}H NMR spectrum. Assignments were achieved via the following steps. First, the proton signals of Ha and H7 for the amide and internal methoxy could be assigned unambiguously to the singlets at 10.93 ppm and 4.01 ppm by comparison with the peaks for all the other amide and internal methoxy protons of SP-1, SP-2 and SP-3 which were observed between 10.8 – 11.0 ppm and 4.10 – 4.00 ppm, respectively.\textsuperscript{35, 58b} The proton signal of H8 for the methylene of benzyl could also be assigned unambiguously to the singlet at 5.20 ppm due to peaks for all the protons of benzyl-containing monomers (S-4, S-8\textsuperscript{*}, S-12\textsuperscript{*}, S-16\textsuperscript{*} and S-20\textsuperscript{*}) observed between 5.02 – 5.13 ppm. The integrations for Ha, H7 and H8 also matched 5, 10 and 15 protons, respectively. The carbon signal at 162.22 ppm could also be assigned unambiguously to C9 by comparison with the carbonyl carbons of SP-1, SP-2 and SP-3 observed between 162.91 – 162.33 ppm.\textsuperscript{35, 58b} The carbon signals of C7 and C8 were assigned at 63.57 ppm and 70.62 ppm, respectively according to correlation in the HSQC spectrum. Based on integration of 5 protons and correlation in the COSY spectrum, the downfield doublet at 8.72 ppm was assigned to H3 or H5 and the doublet at 7.59 ppm was definitely assigned to the other pair. According to correlation between the carbon signal of C9 and the proton signal of H3 in the HMBC spectrum, the
doublets at 8.72 ppm and 7.59 ppm were assigned to H5 and H3, respectively as correlation between C9 and H3 and no correlation between C9 and H5 were observed. Therefore, the other proton signal at 7.59 ppm could be assigned to H5. Based on the HSQC spectrum, the carbon signals at 111.09 ppm and 111.60 ppm could be assigned to C3 and C5, respectively and correlation between Ha and C5 in the HMBC spectrum also agreed. The proton signals in the aromatic region (7.5 ppm) could be assigned to the benzyl protons. Based on integration of 5H, the doublet at 7.36 ppm could be assigned to H13. The carbon signal of C13 was at 128.25 ppm according to correlation in the HSQC spectrum. The other doublet at 7.51 ppm could be assigned to H11 which was integrated 10 H. The carbon signal of C11 was at 127.70 ppm according to correlation in the HSQC spectrum. The remaining triplet at 7.43 ppm could be assigned to H12 which was also integrated 10 protons. The carbon signal of C12 was at 128.78 ppm according to correlation in the HSQC spectrum. The remaining quaternary carbons (C1, C2, C4, C6 and C10) were assigned according to the HMBC spectrum. Based on correlation between the signals of H3, H5 and H7 and the signal of C1, the carbon signal at 140.81 ppm could be assigned to C1. The carbon signal at 136.61 ppm was assigned to C10 due to correlation between the signals of H8 and H12 and the signal of C10. Based on correlation between the signals of H3, H5 and H8 and the signal of C4, the carbon signal at 156.54 ppm could be assigned to C4 although the correlation between the signals of H3 and H5 and the signal of C4 were insufficiently strong. The last two signals for quaternary carbons at 133.70 ppm and 126.02 ppm were C2 or C6. Due to no correlation signals observed in the HMBC spectrum, C2 and C6 could not be assigned. In addition to NMR spectroscopy, its ESI mass spectrum shows the peak at 1298.4362 m/z which can be assigned to [M+Na]^+. 
Figure 2.38. a) $^{13}$C and b) $^1$H NMR spectra of SP-4* in CDCl$_3$.

Figure 2.39. Selected region of COSY spectrum of SP-4*. 
The next step was the benzyl de-protection of SP-4*. The same de-benzylation was accidently achieved by hydrogenation using palladium on carbon as a catalyst at 40 °C and 450 kPa for 18 hours in the previous step where the nitro group in S-16* was reduced to amine. However, O-protecting benzyl groups on SP-4* could not be removed by hydrogenation under any conditions: varying catalysts (palladium on carbon and/or platinum on carbon), temperature up to 50 °C, pressure of H₂ up to 500 kPa and reaction time up to 48 hours. As observed in bromination of SP-1, inertness of SPs was much more challenging for the further reactions.
Boron tribromide (BBr₃) is occasionally used for de-benzylation. Using 5 equivalents of BBr₃ to SP-4* the benzyl groups were successfully removed and yielded hydroxyl-SP (SP-5*) confirmed by ESI mass spectrometry. In Figure 2.42 peaks at 824.1924 m/z for [M-H]⁻, at 810.1895 m/z for [M-CH₃]⁻, at 796.1742 m/z for [M+H-2CH₃]⁺, at 782.1601 m/z for [M+2H-3CH₃]⁺, at 768.1457 m/z for [M+3H-4CH₃]⁺ and at 754.1295 m/z for [M+4H-5CH₃]⁺ in negative ionisation as well as peaks at 848.2013 m/z for [M+Na]⁺, at 834.1867 m/z for [M-CH₃+H+Na]⁺, at 820.1722 m/z for [M-2CH₃+2H+Na]⁺, at 806.1564 m/z for [M-3CH₃+3H+Na]⁺, at 792.1428 m/z for [M-4CH₃+4H+Na]⁺ and at 778.1238 m/z for [M-5CH₃+5H+Na]⁺ in positive ionisation were observed. No peaks for benzyl containing SPs were found, confirming that all the benzyl groups were successfully removed. Purification of SP-5* was successfully achieved by preparative reverse-phase HPLC eluted with 100% of water for 5 min and 0 – 100% of methanol for 25 minutes to give a white solid. The other isomers that lost one or two inner methyls from methoxy could be separated out during the HPLC purification. Since I only have a small amount of SP-5* (approximately 1 µg), substitution of SP-5* with carboxylic acids to synthesise SP-6 has not yet been carried out.
Figure 2.42. ESI-MS spectra of SP-5* in negative (top) and positive ionisation (bottom).
The internal F-macrocycle **SP-7** was successfully synthesised via only two steps, including a new one-pot synthesis (Scheme 2.15). The commercially available starting material, 2-fluoro-3-nitrobenzoic acid, was reduced to 3-amino-2-fluorobenzoic acid (**S-22**) which was then cyclised using phosphoryl trichloride and trimethylamine in dry acetonitrile with stirring at room temperature overnight to give pink precipitate. This reaction condition has been used for the methoxy SP syntheses (**SP-1, SP-2, SP-3** and **SP-4**). The crude product was then washed with methanol, DMF and dichloromethane to give a white solid. The characterisation by NMR spectroscopy and ESI mass spectrometry corresponded to the literature values.\(^{59b}\)

Due to its poor solubility and inertness, bromination of **SP-7** using N-bromosuccinimide under various conditions has not yet been successful. Therefore, a pre-synthesis derivatisation method to synthesise fluoro-Singapore Pentamer substituted with linkers was carried out (Scheme 2.16). Cyano group was selected as a linker. Carboxylic acid is the major functionality for cyclisation where amine and carboxylic acid react and bind to form amide. Having two carboxylic acid groups in the monomer precursor will produce polymeric mixtures rather than Singapore Pentamers. The protected carboxylic acid might lose the protecting group during the multiple steps to the monomer precursor. The pyridyl group was excluded since synthesis of alkylated-pyridyl boronic acid was not carried out in this project. Suzuki cross coupling was a key reaction to substitute a linker onto the monomer intermediate. It was successfully achieved to yield **S-25** and the product was fully characterised by NMR spectroscopy and ESI mass spectrometry.
Scheme 2.16. Proposed reaction scheme for the synthesis of SP-8.
* denotes compounds prepared in this thesis.

The next step, de-esterification of S-25* to yield S-26* using aqueous base was achieved by stirring at room temperature overnight. ESI-MS confirmed the presence of S-26*. The crude product has been purified several times by silica column chromatography but still impure with by-products. Optimisation of eluent conditions is required. The product containing nitro and carboxylic acid was too polar to be moved on a silica column eluted with methanol, not dichloromethane and/or ethyl acetate. The cyano group was so reactive that hydrolysis occurred on the cyano to yield a mixture of amide and carboxylate ammonium species when heat was introduced. The following steps, reduction of the nitro group and cyclisation, are expected to produce another 5*-tile of flat Singapore Pentamer.
substituted with cyano groups as linkers (SP-8). The tert-butyloxy functionality will allow SP-8 to be dissolved in common organic solvents such as ethyl acetate and methanol.

### 2.2.2.2 3*- and 2*-Singapore Pentamers

![Reaction scheme for the synthesis of SP-3, SP-a ~ SP-f and SP-1](image)

Scheme 2.17. Reaction scheme for the synthesis of SP-3, SP-a ~ SP-f and SP-1.\(^{58b}\)

Instead of a chain-extension technique, Huaqiang Zeng’s group has reported one-pot synthesis using a mixture of S-17 and S-19 precursors to produce the series of octyloxy-SPs substituted with a different number of corresponding functionalities (Scheme 2.17). The series of octyloxy-SPs of SP-3, SP-a ~ SP-f and SP-1 were separated by flash silica column chromatography (eluent: ethyl acetate : dichloromethane = 1:50 to 1:10) in the order of SP-3, SP-a ~ SP-f and SP-1 and fully characterised by NMR spectroscopy and ESI mass spectrometry.

In this project the methoxy precursor (S-18) was used to synthesise a mixture of the series of methoxy-SPs substituted with a different number of corresponding functionalities (Scheme 2.18). The \(^1\)H NMR spectrum of the mixture of the series of methoxy-SPs (Figure 2.43b) shows the presence of peaks for the two amide protons, the five aromatic protons and the three methoxy protons, confirming that the H-aromatic bases and methoxy-substituted aromatic bases were present and their adjacent aromatic bases were same and/or different. For example, the order of the aromatic bases can be H-H-H, H-OCH\(_3\)-H, H-OCH\(_3\)-OCH\(_3\), OCH\(_3\)-OCH\(_3\)-OCH\(_3\) and so on. The peak-broadening could also account for
the mixture nature of the different numbers of substituents. The ESI mass spectrometry (Figure 2.44 and Table 2.2) of the resulting product also agreed with the presence of the series of methoxy-SPs by the observation of the peaks at 902.2775 m/z for [SP-2-OCH₃+K-H]⁺, at 872.2189 m/z for [SP-2-2OCH₃+K]⁺, at 834.2688 m/z for [SP-2-2OCH₃+H], at 804.2575 m/z for [SP-2-3OCH₃-2H]⁺, at 774.2436 m/z for [SP-2-4OCH₃-3H]⁺ and at 744.2347 m/z for [SP-2-5OCH₃+4H]⁺ in negative ionisation as well as peaks at 888.2655 m/z for [SP-2-OCH₃+H+Na]+, at 858.2596 m/z for [SP-2-2OCH₃+2H+Na]⁺, at 828.2508 m/z for [SP-2-3OCH₃+3H+Na]⁺, at 798.2400 m/z for [SP-2-4OCH₃+4H+Na]⁺ and at 768.2288 m/z for [SP-2-5OCH₃+5H+Na]⁺ in positive ionisation. Purification via flash silica column chromatography eluted with a mixture of ethyl acetate : dichloromethane = 1:50 was carried out and the ¹H NMR spectrum of the collected first fraction (Figure 2.43a) was identical to that of SP-1. Presumably, the separation order of the mixture of the methoxy isomers by flash silica column chromatography was reversed and the order of the fractions could be SP-1, SP-9f ~ SP-9a and SP-2.

Scheme 2.18. Reaction scheme for the synthesis of SP-2, SP-9a ~ SP-9f and SP-1.⁵⁸b
<table>
<thead>
<tr>
<th>Positive ionisation</th>
<th>Negative ionisation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formula</strong></td>
<td><strong>Mass (m/z)</strong></td>
</tr>
<tr>
<td>[SP-2-2OCH₃+2H+Na]⁺</td>
<td>858.2596</td>
</tr>
<tr>
<td>[SP-2-3OCH₃+3H+Na]⁺</td>
<td>828.2508</td>
</tr>
<tr>
<td>[SP-2-4OCH₃+4H+Na]⁺</td>
<td>798.2400</td>
</tr>
<tr>
<td>[SP-2-5OCH₃+5H+Na]⁺</td>
<td>768.2288</td>
</tr>
</tbody>
</table>

Table 2.2. Formulas and mass values for the reaction mixture for SP-2, SP-9a ~ SP-9f and SP-1 found in ESI-MS.

Figure 2.43. ¹H NMR spectra in CDCl₃ of a) SP-2, b) SP-1, c) the crude mixture of SP-2, SP-9a ~ SP-9f and SP-1 and d) the 1ˢᵗ fraction from the mixture of SP-2, SP-9a ~ SP-9f and SP-1.
Figure 2.44. ESI-MS spectra of the series of methoxy-SPs of SP-2, SP-9a~SP-9f and SP-1 in negative (top) and positive ionisation (bottom).

The drawback of this purification of those chemically similar compounds was not only sensitivity of the eluent ratio, but also the colour of the isomers. Due to the white colour of Singapore Pentamers,
invisibility of the fractions of the series of methoxy-SPs on the silica column rendered the isolation of each product even harder. Multiple attempts of the flash silica column chromatography and a great chromatography skill were essential for successful isolation of each of the product. This isolation of SP-2, SP-9a ~ SP-9f and SP-1 has not yet been completed.

Moreover, when the fluoro-cyano-monomer precursor (S-27) is successfully synthesised and well characterised, one-pot synthesis of 2*- and 3*-fluoro-Singapore Pentamers can be carried out. This fluoro-cyano system does not require further linker-attaching reactions. Their flat structural geometry will be an advantage on deposition. If isolation of each product synthesised by the one-pot synthesis method is problematic, the chain-extension method can be an alternative.

2.3 Supramolecular building blocks

Calix[5]arenes and [5]cavitands cannot be good candidates for Penrose tiling since their “truncated cone shape” structures allow substitution on their portals, not on their sides. Two dimensional extension of Penrose tiling of those building blocks via intermolecular hydrogen bonding or metal coordination through linkers on the portals of calix[5]arenes and [5]cavitands will be challenging. Portal to portal networks tend to grow vertically, not horizontally and this vertical growth will give rise to even more complicated intermolecular binding networks. For example, if linkers are attached on only one side of the portals, it is likely to form the alternative up-and-down network as shown in Figure 2.45b rather than one-sided network like Figure 2.45a. If the linkers are attached on both sides of the portals, its geometry could be more complex and become 3D network as shown in Figure 2.45c which would be impossible to induce to form molecular Penrose tiling production. Therefore, in this thesis calix[5]arenes and [5]cavitands were not studied. Cucurbit[5]uril with a “pumpkin shape” which can be functionalised on its side was used as a tile for Penrose tiling.

The largest tile in this project is cucurbit[5]uril which was first isolated by Kimoom Kim and his colleagues in 2000. The first report of CB[6] was in 1905 by Behrend and due to its large cavity inclusion properties have been well-studied by Mock and Shih. Therefore, host-guest chemistry of CB[6] has also been widely explored. Since other homologues, CB[5,7,8], were isolated by Kimoom Kim’s group (Figure 2.46), these homologues have been used for diverse applications; for example, biomedical applications, chiral applications, supramolecular architectures, supramolecular analytical applications, and nanostructured materials. Functionalization of CBs was a great achievement not only for synthetic chemistry of CBs but also for exploring a variety of applications such as artificial ion channels, vesicles, stationary phases in chromatography, ion selective electrodes, polymers, nanomaterials, waste water treatment, drug/gene delivery, immunization, catalysis, sensors, biochips, separation of biologically important molecules, odour removal, slow release of fragrance, and reduction of toxicity of anticancer drugs.
CB[5] is composed of five equivalents of glycoluril and ten methylene bridges. Its ureidyl-carbonyl portals are hydrophilic and tend to coordinate alkali ions whereas the central cavity is hydrophobic and thus CBs can carry a hydrophobic guest in aqueous solution.\cite{75} Due to its smaller cavity, CB[5] can only encapsulate gas molecules such as N\textsubscript{2}, O\textsubscript{2} and Ar. It also binds NH\textsubscript{4}\textsuperscript{+} to the portals and can close one of the openings whereas CB[6] can encapsulate a larger molecule, such as 1,4-diaminobutane.\cite{74}

For this project we synthesised and substituted CB[5] with linkers (carboxylate, cyano and pyridyl groups). As hydrolysis of CBs to form hydroxy-CBs has been reported, the direct functionalisation of CBs is feasible. Further substitution of hydroxyl-CBs with the linkers using boronic acids is explored in this thesis. The boronic acids used in this project were 4-borobenzoic acid, pyridin-4-ylboronic acid and (4-cyanophenyl)boronic acid which are commercially available. 4-Borono-2-butylbenzoic acid (B-1) which was synthesised in this thesis was also used to improve the solubility of the resulting product.

Preparation and isolation for CB[5] have been reported by Kimoon Kim’s group.\cite{64} We synthesised CB[5] and functionalised CBs with the generous support from Dr. Narayanan Selvapalam (Kimoon Kim’s group) who has developed the preparation for CB[5 and 6] described in this thesis. A mixture of glycoluril and 1.3 equivalents of 35% aqueous formaldehyde in a 1:1 mixture of water to concentrated sulfuric acid was stirred at 105 °C overnight. The heating was to allow the water to evaporate slowly and CB[6] slowly precipitated out since CB[6] is soluble in sulfuric acid but not in

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**Figure 2.46.** X-ray structures of CB[5-8]. C = grey, N = blue, O = red. (reproduced from ref. 74)
concentrated sulfuric acid. The CB[6] was collected by filtration and washed thoroughly with water to give a white solid. The filtrate contained the other homologues. Polymeric species from the filtrate precipitated out by adding twice volume of water and six times volume of acetone to the filtrate and removal by filtration. The collected large volume of the filtrate was stored for days to grow crystals of CB[5].

Figure 2.47. $^1$H NMR spectra of a) CB[6] (top) and CB[6] with 1,4-diaminobutane (bottom) in D$_2$O/D$_2$SO$_4$ and b) CB[5] (top) and CB[5] with 1,4-diaminobutane (bottom) in D$_2$O. All spectra were calibrated by TSP (Trimethylsilyl propanoic acid).
The $^1$H NMR spectroscopy of CB[5 and 6] with 1,4-diaminobutane confirmed the difference between CB[5] and CB[6] in the size of cavity. Assignment of the proton signals was achieved by comparison with the literature values.\textsuperscript{64} Figure 2.47 demonstrates that 1,4-diaminobutane can be encapsulated by CB[6] and this encapsulation results in chemical shifts of both the host and guest, whereas no chemical shift was observed in the$^1$H NMR spectra of CB[5] with 1,4-diaminobutane. In Figure 2.47a, the peaks for the 1,4-diaminobutane were guest at 2.05 ppm for the 1,4-CH$_2$ and 0.36 ppm for the 2,3-CH$_2$. In addition, the peaks for the CB-CH$_2$ bridges and glycoluril units were shifted downfield. In contrast, Figure 2.47b showed that no peaks for inserted 1,4-diaminobutane were observed and the peaks for the CB-CH$_2$ bridges and glycoluril units remained the same in the presence and absence of 1,4-diaminobutane. Integration of the peaks of CB[6] and the inserted 1,4-diaminobutane did not match since it is common that peaks for encapsulated guests cannot be fully detected. More likely, under acidic conditions, 1,4-diaminobutane could be converted into the $n$-butyldiammoium salt which acted as an intermolecular bridge as shown in Figure 2.48. These dimer/oligomer species have the same characteristics in $^1$H NMR spectroscopy as free CB[6] and 1,4-diaminobutane. The peaks for free CB[6] and 1,4-diaminobutane as well as the dimer/oligomer species can be observed at the same locations and therefore integration of those peaks of CB[6] and inserted 1,4-diaminobutane could not be matched. For improvement of solubility of CB[6] a small amount of D$_2$SO$_4$ was added and the deuterated acid caused the D$_2$O peak splitting in Figure 2.47a.

![Figure 2.48](image-url)  
Figure 2.48. Intermolecular dimerization/oligomerisation of CB[6] bridged by $n$-butyldiammoium salts under acidic condition. $n \geq 0$.

CB[6] can be the best model compound for the CB[5] tiling. Chemical properties of CB[5 and 6] are quite similar. For example, according to the literature,\textsuperscript{76} further functionalization of CB [5, 6, 7 and 8] are carried out under the same condition and the yields of CB[5 and 6] products are 42% and 45%, respectively, whereas for the CB [7 and 8] products the yields are in 5% and 4%, respectively. More importantly, during the reaction of CBs CB[6] is produced in about 80 – 90 % although CB[5] is very low yielding (about 2%).

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2.3.1.1 5*-CB[5]

Scheme 2.19. Direct functionalization of CBs.

Direct functionalisation of CB[5] allows synthetic accessibility of the 5*-CB tile (Figure 2.49). Using potassium persulfate as oxidant, hydroxy groups were added to the glycoluril units of CB[5] after heating at 85 °C for 12 h. The potassium salt intermediate species (Scheme 2.19 middle) with a lot of by-product, potassium sulfate, was firstly isolated as a white powder. After addition of concentrated H₂SO₄ to a solution of the intermediate salt, most of the potassium sulfate was removed and relatively pure decahydroxy-cucurbit[5]uril (CB[5](OH)₁₀) was produced. Although this final product still contains some occluded K₂SO₄ and H₂SO₄, subsequent alkylation and boronation reactions were carried out without further purification.
Scheme 2.20. Allylation (top) and boronation (bottom) of CB[5 and 6].

One of the advantages to functionalising CBs is the enhancement of their solubility. CB[6] is soluble in only acidic media. Both neutral and acidic water can dissolve CB[5]. However, DMSO and DMF can dissolve the hydroxy-CB[5 and 6]. The allyloxy-CBs and the boronated-CBs can be dissolved in methanol. The boronated-CBs were designed for this project (Scheme 2.20). As shown in Figure 2.50, peaks of CB[6] bridges were shifted; Ha to downfield and Hb to upfield. COSY correlations of those peaks for CB[6](Oallyl)_{12} agreed with the assignment. ESI-MS also confirmed the successful production of CB[6](Oallyl)_{12}. The collected characterisation data corresponded to the literature values. This solubility improvement is promising that substituted-CB tiles can be used for liquid-phase deposition.
The allyloxy-CBs have been reported by Kimoon Kim’s group.\textsuperscript{76} CB[6](Oallyl)\textsubscript{12} was re-synthesised in this project to experience further functionalisations of hydroxy-CB[5 and 6] and to investigate nature of the alkylated-CB. Deprotonation of CB[6](OH)\textsubscript{12} by sodium hydride, followed by addition of allyl bromide gave CB[6](Oallyl)\textsubscript{12} as a light brown solid. As the model study with CB[6](OH)\textsubscript{12} which was used as a precursor for the allylation, it was confirmed that hydroxyl-CB[5 and 6] impure with inorganic salts can be used for further reactions. Therefore, attempts to synthesise 5*-tiles by condensation using boronic acids which contained linkers were carried out. The boronic acids used in this project were pyridin-4-ylboronic acid, (4-cyanophenyl)boronic acid, 4-boronobenzoic acid and 4-boronobutylbenzoic acid (B-1). The major reason for selecting those boronic acids was that since CB[5](OH)\textsubscript{10} contained ten active-binding sites and to be a 5*-tile only five linkers had to be attached on the tile, those commercially available boronic acids are ideal reagents to convert CB-tiles containing ten binding sites into 5*-CB[5] tiles. Phenyl boronic acid was also used as a model for these boronation reactions. Furthermore, the hygroscopic nature of DMSO used as a solvent contributed to the reaction going forward by absorbing the H\textsubscript{2}O by-product.
As shown in Figure 2.51, instead of OHs on one glycoluril unit reacting with one boronic acid, one each of OH from two adjacent glycoluril bodies reacting with one boronic acid can be a concern. If the condensation occurs between two glycoluril units, no means of controlling reaction directions for boronic acid and the glycoluril body in ratio of between one-to-one and one-to-two results in a total mixture of CBs with randomly attached boron groups. However, in X-ray crystallography of CB[6](OH)$_{12}$ the distance between hydroxy-oxygens in two adjacent glycolurils (3.92 Å in average) is larger than the distance between hydroxy-oxygens in one glycoluril (2.76 Å in average). Moreover, the distance between hydroxy-oxygens in two adjacent glycolurils in CB[5](OH)$_{10}$ (4.43 Å in average) is even larger. For comparison, the distance between oxygens on O-B-O of the mannitol tris(benzeneboronic) ester molecule$^{77}$ is 2.29 Å and those of 1,4-phenylenediboronic acid$^{78}$ is 2.31 Å (Figure 2.52). Therefore, boronic acids are more likely to react with the OHs on one glycoluril unit of CB[5 or 6].

Figure 2.51. Illustration of reaction geometry of phenyl boronic acid with the two OHs from two neighbouring glycolurils in CB[5].
Figure 2.52. Structures of mannitol tris(benzeneboronic) ester and 1,4-phenylenediboronic acid.\textsuperscript{77-78}

![Mannitol tris(benzeneboronic) ester](image)

![1,4-Phenylenediboronic acid](image)

Scheme 2.21. Reaction equilibrium of phenylboronic acid and diol ester at different pH.\textsuperscript{79}

However, the reactive nature of the boronated products in solution resulted in difficulties in purification and characterisations of the final products. In Scheme 2.21 the condensation of boronic acid and diol ester is a reversible reaction which is most likely to end up with a mixture of the product and starting materials. This pH-dependant equilibrium was observed in this project where over time the boronated products in aqueous solution were degraded back to a mixture of hydroxy-CBs and corresponding boronic acids which precipitated out as white powders. Moreover, the borate product in anionic form is not symmetric due to the extra OH groups which can be attached on boron in random directions as shown in Figure 2.53 and therefore analysis of NMR spectra of those products is another challenge.
The boronated-CBs were prepared by the following description. A mixture of the hydroxyl-CBs and the boronic acid reagents in DMSO was stirred at room temperature for 5 hours. Addition of a large volume of diethyl ether to the reaction mixture gave a white precipitate which was washed at least three times with diethyl ether and acetonitrile. The white solid contained the boronated-CBs and potassium sulfate which was from the starting material (hydroxyl-CBs). Due to the equilibrium (Figure 2.53), the boronated-CBs were decomposed during the processes of removing potassium sulfate. Instead of the hydroxy-CBs, the intermediate CBO$\text{K}^+$ species can also be used and the results were the same, although the O$^-$ was more reactive than OH and thus the intermediate CBO$\text{K}^+$ species were expected to be better precursors. Synthesis of CB[5]($\text{O}_2\text{BC}_6\text{H}_4\text{COOH})_n($OH)$_{5-n}$ was carried out using basic buffer aqueous solution with pH 13 as a solvent, instead of DMSO, to improve solubility of the corresponding boron reagent. Neutral water can also be used as a solvent for the boronation reactions using phenyl boronic acid, pyridin-4-ylboronic acid and (4-cyanophenyl)boronic acid as reagents. Easier purification by handling aqueous solvent rather than DMSO benefits from this alternative method. However, the isolation and full characterisation of the 5*-CB[5] tiles still remains unsolved.

Figure 2.53. Possible equilibrium structures of boronated CBs.

\[ \text{R-B-O} \leftrightarrow \text{R-BOH} \]

Figure 2.54. Structure of boronated-CBs. Two possible directions to attachment of OH$^-$. 

$^1$H NMR spectra of CB[6]($\text{O}_2\text{BPh})_6$, CB[6]($\text{O}_2\text{BC}_6\text{H}_4\text{COOH})_6$, CB[6]($\text{O}_2\text{BC}_6\text{H}_4\text{CN})_6$, CB[6]($\text{O}_2\text{BC}_3\text{H}_4\text{N})_6$, CB[6]($\text{O}_2\text{BC}_6\text{H}_4\text{BuCOOH})_6$, CB[5]($\text{O}_2\text{BPh})_5$, CB[5]($\text{O}_2\text{BC}_6\text{H}_4\text{COOH})_5$, CB[5]($\text{O}_2\text{BC}_6\text{H}_4\text{CN})_5$, CB[5]($\text{O}_2\text{BC}_3\text{H}_4\text{N})_5$, and CB[5]($\text{O}_2\text{BC}_6\text{H}_4\text{BuCOOH})_5$ were almost identical (see Scheme 2.20 for sketches). Two sets of doublets at around 5.5 ppm and 4.5 ppm for the CBCH$_2$-
bridge protons and another two sets of doublets at around 7.5 ppm for the phenyl or pyridyl protons are expected to be observed. However, as an example shown in Figure 2.55, four or six sets of broad doublets or singlets for the CB-bridge protons were observed at around 5.5 ppm and 4.5 ppm. Broad doublets or singlets (3 – 5 sets) for the phenyl or pyridyl protons were observed at around 7.5 – 8.5 ppm. The number of phenyl or pyridyl peaks were usually four (two for free boronic acid and the other two for the corresponding boron substituents). Sometimes, those peaks overlapped and became three peaks in total. Occasionally, a singlet of an impurity peak was observed at about 8.15 ppm. The shifting and varying intensities of the peaks could be associated with the equilibrium nature of boron in solution and the presence of free boronic acid acting as a Lewis acid which changes pH of the solution. Although the locations of those peaks were at the right positions, the peak splitting and integration of those peaks still question whether the fully substituted products in the borate forms were homogeneous but asymmetric (Figure 2.54) or the peak splitting and unmatched integration resulted from a mixture of partially substituted- and fully substituted products. Randomly attached OHs in the borate forms could break the symmetry of the fully substituted products, causing the split peaks for CB-CH$_2$ protons in the $^1$H NMR spectra.
Figure 2.55. $^1\text{H}$ NMR spectra of CB[5](O$_2$BC$_6$H$_4$COOH)$_{10}$ in MeOD (top), d$_6$-DMSO (middle) and D$_2$O (bottom).

The $^{11}\text{B}$ and DOSY NMR spectroscopy agreed that the carboxy-phenyl borons were attached onto CB[5] instead of a mixture of the two unreacted starting materials. In the $^{11}\text{B}$ NMR spectrum (Figure 2.56a) the boron peak for 4-boronobenzoic acid was found at 3.31 ppm whereas the peak for boron substituted onto CB[5] was observed at 28.83 ppm and was broadened. This broadening is often observed for coordinated borons in $^{11}\text{B}$ NMR spectroscopy. The DOSY NMR spectroscopy showed separate peaks for different molecules which have different diffusion coefficients. In Figure 2.56 the peak at around -9.59 log(m$^2$/s), -9.32 log(m$^2$/s) and -8.73 log(m$^2$/s) could be assigned to CB[5](O$_2$BC$_6$H$_4$COOH)$_5$ in the red box, free 4-boronobenzoic acid in the brown box and water in the green box, respectively. According to Figure 2.56b, the aryl peaks for CB[5](O$_2$BC$_6$H$_4$COOH)$_5$ were slightly shifted upfield, compared to aryl peaks for free 4-boronobenzoic acid. According to the DOSY NMR spectrum, unreacted 4-boronobenzoic acid was present. This also implies that the partially substituted CB[5] tiles and free CB[5](OH)$_{10}$ could be present. It is likely that the peaks could overlap at around -9.59 log(m$^2$/s) as the diffusion coefficients of the fully- and partially-substituted
CB[5](O₂B₆H₄COOH)₅(OH)₅₋₅ and CB[5](OH)₁₀ are expected to be quite close to each other. The boron-linker substitution onto CB[5] has occurred although these ¹¹B and DOSY NMR spectroscopy could not clarify whether the product was a homogeneous CB[5](O₂B₆H₄COOH)₅ or a mixture of the fully- and partially-substituted CB[5](O₂B₆H₄COOH)₅(OH)₅₋₅ and CB[5](OH)₁₀.

![Figure 2.56. a) ¹¹B NMR spectra of 4-boronobenzoic acid (top) in D₂O and CB[5](O₂B₆H₄COOH)₅ in MeOD and b) DOSY spectrum of CB[5](O₂B₆H₄COOH)₅. CB[5](O₂B₆H₄COOH)₅ in the red box, free 4-boronobenzoic acid in the brown box, water in the green box; impurities marked ×.](image)

Although the peaks for fully substituted CBs bearing five aryl borons were found in the MALDI-TOF spectra, the presence of partially substituted products could not be confirmed since peaks for partially substituted CB products observed in their MALDI-TOF spectra could be from either the actual products substituted partially or fractions of the fully substituted product. For example, in Figure 2.57a the peaks for CB[5](O₂B₆H₄COOH)₅ ionised with potassium ion could be assigned at 1679.37 m/z and the peaks at 1587.31 m/z, 1457.27 m/z, 1327.24 m/z, 1197.21 m/z and 1067.18 m/z could also be assigned to CB[5](OH)₂(O₂B₆H₄COOH)₄, CB[5](OH)₃(O₂B₆H₄COOH)₃,
CB[5](OH)₆(O₂BC₆H₄COOH)₂, CB[5](OH)₈(O₂BC₆H₄COOH) and CB[5](OH)₁₀ ionised with two potassium ions and loss of one proton, respectively. Figure 2.57b also showed the peaks for CB[5](O₂BC₅H₄N)₅, CB[5](OH)$_2$(O₂BC₅H₄N)$_4$ and CB[5](OH)$_4$(O₂BC₅H₄N)$_3$, respectively. Furthermore, the peaks for the fully substituted product ionised with potassium ion was found in the MALDI-TOF spectrum of CB[5](O₂BC₆H₄CN)$_₅$. With regards to intensity of the peaks, the fully substituted CB product, CB[5](O₂BC₅H₄N)$_₅$, was dominant in Figure 2.57b. Although mass spectrometry is not a quantitative analysing tool, these results of MALDI-TOF mass spectrometry are promising that the major products could be the fully substituted CBs.
2.3.1.2 3*- and 2*-CB[5]

Flinn and co-workers have reported synthetic methodology of exclusive CB[5](Me)_{10} which is derived from a reaction of dimethyl glycoluril with formaldehyde in conc. hydrochloric acid under reflux (Scheme 2.22). After gradually cooling to room temperature, white powder of the pure product CB[5](Me)_{10} precipitates out in 16% yield which was based upon the result produced in this thesis. Based on the low yield of CB[5](Me)_{10}, other homologues could also be produced but remain in the acidic medium. Compared to CB[5] which is synthesised in relatively low yield and requires multiple purification processes, the isolation process for CB[5](Me)_{10} which is filtration followed by washing with water is simple and relatively high yielding. The precursor, dimethyl glycoluril, can be
synthesised in a large scale (100 g) using urea and 2,3-butanedione in mild acidic media (quantitative yield based upon the result produced in this thesis).

![Chemical structures and reaction scheme]

Scheme 2.23. Proposed synthesis of 2*- and 3*- CBs.

Theoretically, if a one-to-one ratio mixture of glycoluril and dimethyl glycoluril reacts with formaldehyde, the major products are expected to be 2*- and 3*- CB-H precursors which hopefully precipitate out as a powder (Scheme 2.23). During the cyclisation reaction, the other isomers and 1*- and 4*- CB-H precursors that must also form as shown in Figure 2.58 precipitate with 2*- and 3*- CB-H precursors. Active binding sites of those isomers are adjacent to one another. As long as all precipitate is CB[5] analogues, the process of separating unwanted homologues such as methyl-CB[6,7,8] can be eliminated. Isolation of the 2*- and 3*- CB-H precursors from the other isomers and 1*- and 4*- CB-H precursors (Figure 2.58) by flash column chromatography or recrystallization might be possible. However, it was unfortunate that after cooling to 0 °C, no precipitate was observed. Addition of acetone into the reaction mixture gave off-white precipitate which was a mixture of CB homologues with/without methyl substituents, according to the 1H NMR spectra in Figure 2.59. Those analogues of each homologue have not yet been isolated.
2.4 Syntheses of linker-substituted boronic acids

Linker-substituted boronic acids are the key reagents that utilise the macrocyclic/supramolecular building blocks with 5-fold symmetry via Suzuki cross-coupling and condensation to produce 5*-?, 3*-?, and 2*-tiles. Pyridin-4-ylboronic acid, (4-cyanophenyl)boronic acid and 4-boronobenzoic acid are commercially available. Campestarenes and Singapore Pentamers that were derived from Suzuki cross-coupling consisted of biphenyl units. Their solubilities in common organic solvents were extremely poor and only DMSO and DMF can dissolve those macrocycles. To improve the solubility
of those biphenylmarcrocycles substitution of the aryl boronic acid with an alkyl chain was required and designed for this project (Scheme 2.24 and Scheme 2.26).

Scheme 2.24. Synthesis of alkyl substituted 4-boronobenzoic acid (B-1 and B-2).82

Mono-alkylation was undertaken using a Grignard reagent which was prepared from mixing magnesium turnings and alkyl bromide under reflux. If length of the alkyl chain is too short, solubility of the macrocycles will be still poor and if alkyl chains are too long, they will dominate the orientation of tiles in a monolayer and linkers will not function properly. Therefore, n-butyl and n-heptyl chains have been selected in this system. Although 3 equivalents of the Grignard reagents were added to 4-bromo-2-fluorobenzoic acid, mono-alkylation selectively occurred on the ortho- position where fluoride was removed. The mono-substituted products were characterised by NMR spectroscopy and ESI mass spectrometry. In particular, ESI mass spectrometry double-confirmed that the products contained bromine which has a distinctive isotope pattern. Unreacted 4-bromo-2-fluorobenzoic acid was recovered during flash silica column chromatography for purification of the products.

Figure 2.60. $^{11}$B NMR spectra of 4-borono-2-butylbenzoic acid B-1 (top) and 4-borono-2-heptylbenzoic acid B-2 (bottom).
The following conversion of the aryl halides into arylboronic acids was achieved by using triisopropyl borate and n-butyllithium. According to the literature reported by Li and colleagues, sequential addition of n-butyllithium followed by triisopropyl borate to the alkyl-aryl halides gives better yields.\(^8\)

In addition, 4-borono-2-butylbenzoic acid \(\text{B-1}\) which is substituted with the shorter alkyl chain (38.89% yield) was produced in higher yield than 4-borono-2-heptylbenzoic acid \(\text{B-2}\) which contains the longer alkyl chain (25.67% yield). The products were characterized by NMR spectroscopy and ESI mass spectrometry. In particular, the \(^{11}\)B NMR spectra clearly showed boron peaks at 18.547 ppm for 4-borono-2-butylbenzoic acid \(\text{B-1}\) and 18.767 ppm for 4-borono-2-heptylbenzoic acid \(\text{B-2}\) (Figure 2.60). Moreover, corresponding results with distinct boron isotope patterns in ESI mass spectrometry for the boron containing products also agreed that conversion has occurred and the products have been well isolated (Figure 2.61).

Scheme 2.25. Alkylation of 4-bromo-2-fluorobenzonitrile using Grignard reagent.
In contrast, alkylation for cyano-substituted phenylboronic acid using Grignard reagent was difficult due to unwanted alkylation that occurred on the cyano group as shown in Scheme 2.25. Therefore, instead of Grignard alkylation, addition of alkoxide to 4-bromo-2-fluorobenzoic acid was conducted (Scheme 2.26). Since nitrile-containing compounds are more soluble in common organic solvents (except for DMSO and DMF) than carboxyl-containing compounds, tert-butoxide was considered to be sufficient for campestrarenes and Singapore Pentamers.

Scheme 2.26. Synthesis of (3-(tert-butoxy)-4-cyanophenyl)boronic acid B-3.

With respect to conversion of aryl halide into arylboronic acid, *in-situ* addition of *n*-butyllithium to a mixture of triisopropyl borate and 4-bromo-2-(tert-butoxy)benzonitrile (B-3a) gave better yield, according to the literature. Although the yield of the product (29%) was not as high as 4-borono-2-butylbenzoic acid B-1 (39%), (3-(tert-butoxy)-4-cyanophenyl)boronic acid B-3 was successfully synthesised and characterised by NMR spectroscopy and ESI mass spectrometry. In particular, a peak for the product at 18.544 ppm was observed in the $^{11}$B NMR spectrum and its corresponding ESI mass spectroscopy where the peak at 218.0993 m/z for [M-H]$^-$ with the distinct boron isotope pattern was observed also confirmed the presence of the final product (Figure 2.62).

Figure 2.62. ESI-MS spectrum of (3-(tert-butoxy)-4-cyanophenyl)boronic acid B-3.
Chapter 3  Preparation of substrates

Selection of substrates is essential for this project. First of all, substrates should be able to adhere the tiles strongly enough that the tiles are not detached. Secondly, the tiles need to be able to re-assemble and correct themselves to form Penrose tiling since the tiles are more likely to randomly deposit on a substrate, not in quasicrystalline ordering. That is, the pentagonal molecules must be attached on substrates but not too strongly. Lastly, the pentagonal molecules should deposit ‘flat’ on substrates, not ‘edge-on’ or ‘tilted’. Furthermore, monolayers of Penrose tiling should form, not multilayers since self-assembled molecular quasicrystals have not yet been reported and without any database of molecular quasicrystals it will be quite challenging to characterise multilayers of quasicrystals. The first characterisation tools for molecular Penrose tiling are STM (Scanning Tunneling Microscope) and AFM (Atomic Force Microscopy). Once monolayers of molecular Penrose tiling have been sufficiently characterised by STM and AFM, further studies of the monolayers of molecular Penrose tiling can be conducted.

It would be much easier if quasicrystalline substrates are used to generate molecular quasicrystals. If 5-fold symmetric molecules are deposited on quasicrystalline substrates without linkers, the tiles may align with the quasicrystalline template from the substrates and molecular quasicrystals may form. In this case, the major driving force for generating molecular quasicrystals is quasicrystalinity of the substrates and the product is not actually self-assembled tiling since there is no interaction between the tiles. It might be difficult to grow multilayer and/or 3D materials.

One of the key factors for generating molecular Penrose tiling is smoothness of surfaces of substrates. The production of a thin film of a monolayer of molecular Penrose tiling where intermolecular bonding is relatively weak requires atomically smooth surfaces due to the expected intolerance of distortion in such a complex system of ordering. Surface smoothening processes such as annealing may be necessary in order to avoid rough surfaces. The most commonly and widely used substrates that can achieve atomically smooth surfaces are gold, HOPG (Highly Ordered Pyrolytic Graphite) and mica.

AFM is a technique for analysing the surface of a material down to nano scale. Deflection occurs on a cantilever by forces between a tip and a surface and the deflection of the cantilever is measured using a laser spot reflected from the top surface of the cantilever into an array of photodiodes. AFM can be the most efficient tool that monitors smoothness of surfaces at an atomic level. However, STM where
voltage difference is applied between a conducting tip and a surface and electrons are allowed to tunnel between them cannot be applicable to mica which does not have conductivity. Therefore, typically a metal is deposited on mica and used as a metal substrate, for example gold on mica.

The size of flat surfaces is also important to observe the quasicrystalline pattern. A reasonable number of tiles to be able to demonstrate molecular Penrose tiling is estimated to be around 50 which are well-connected in an ordered array. The size of tiles and length of linkers are the major factors for deciding the minimum size of a flat surface. A reasonable size of an atomically flat surface for Penrose tiling comprised of the small tiles, croconate and pentacyanocyclopentadiene, is at least $10 \text{ nm} \times 10 \text{ nm}$. This is based on a mathematical estimation in which the size of cyclopentene would be approximately $0.5 \text{ nm} \times 0.5 \text{ nm}$ and length of the linker (carbonyl – metal – carbonyl or cyano – metal – cyano) would be approximately $0.5 \text{ nm}$. In case of the macrocycles categorised in the medium tiles, Singapore Pentamer and campestarene, the pentagon block would be approximately $1.3 \text{ nm} \times 1.3 \text{ nm}$ in size and the longest case of its carboxylic acid-carboxylic acid hydrogen bonding would be approximately $1.5 \text{ nm}$ in length. The outer diameter of the large tile, cucurbit[5]uril, is $1 \text{ nm}$ and the linker (the boron functional groups with hydrogen bonding) would be approximately $4 \text{ nm}$ in length. The size of atomically flat surfaces for the medium tiles and the large tile are at least $60 \text{ nm} \times 60 \text{ nm}$ and $100 \text{ nm} \times 100 \text{ nm}$, respectively.

3.1 Gold

Gold is a well-known material as a substrate in surface chemistry. Gold substrates have been well-studied and widely used for the formation of organic monolayers, ultrathin polymer films and well-ordered 2D protein arrays. A great advantage of gold is its chemical inertness. Gold substrates should not react with tiles or linkers. Atomically smooth surfaces of gold are also achievable. Gold on mica with about $300 \text{ nm}$ across atomically flat terraces is commercially available. Moreover, our department has facilities for the production of gold substrates using evaporation technique on base wafers, such as silicon, quartz, glass and mica.
3.1.1 Production

3.1.1.1 Pre-treatment

Base wafers (glass microscope slides, silicon(111) and quartz slides), pure gold (evaporation slug, 99.99% trace metal basis) and pure chromium (chips, 99.995% trace metal basis) were purchased. The base wafers were resized using a diamond scribe. The size of the cut wafer should be around 1 cm × 1 cm where samples can normally fit in sample holders of characterisation instruments. The main purpose for pre-cutting is to minimise contamination. Most contamination occurs in cutting process. If the cutting process is carried out after cleaning in piranha solution or gold deposition, scratches and/or impurities on surfaces are inevitable although larger pieces of wafers are easier to handle.

In order to remove organic contaminants on surfaces, the cut wafers were soaked in a petri dish with piranha solution (a mixture of conc. H$_2$SO$_4$ and 30% H$_2$O$_2$, 3:1) and allowed to stand for a few hours (minimum 1 hour). Meanwhile, bubbles decomposed from organic residues formed on surfaces and need to be removed. After a few hours, wafers were taken out, thoroughly washed with MiliQ water and dried by blowing N$_2$ gas.

Another cleaning process is oxygen plasma cleaning. Oxygen is excited and ionised in vacuum UV. Firstly, vacuum UV breaks organic bonds and large molecules are broken apart. Secondly, activated oxygen species and other species created in vacuum UV (O$_2^+$, O$_2^-$, O$_3$, O, O$^+$, O$^-$, ionised ozone, metastable excited oxygen and free electron) react with the broken atoms and smaller molecules by vacuum UV and form gaseous species under high vacuum system.

3.1.1.2 Thermal evaporation

Thermal evaporation is one of the most useful techniques to produce atomically flat gold films on base substrates. Under high vacuum (below 10 - 7 bar) melted gold vaporises and travels in a bell jar until it encounters a cold surface where gold is condensed. Therefore, gold vapour are evenly distributed in a closed system and equally coat all the surfaces. Overnight vacuum pump running may be needed since the low pressure (below 10 - 7 bar) has to be reached before heating gold. Otherwise, melt gold will not fully evaporate and thin film coating of gold will not be produced. The purchased gold metal is placed in a tungsten basket where current flows through the basket coil and generates heat that melts the metal to be evaporated. Tungsten baskets are used for higher melting point materials instead of
molybdenum boats that have the melting point of 2622 °C. The melting points of tungsten, gold and chromium are 3422 °C, 1064.18 °C and 1907 °C, respectively.

Evaporated gold can adhere to glass, quartz and mica whereas gold on silicon substrates is easily peeled off. Therefore, an adhesion layer between gold and silicon is required for further deposition study. Chromium and titanium can be the best materials for the adhesion layer which effectively adheres to both gold and silicon. Au/Cr/Si and Au/Ti/Si are commonly used as gold substrates.

Chromium was used as an adhesion layer material in this project. Two tungsten baskets, each loaded with a piece of gold and chromium, were clamped and an aluminium foil block was also placed between the two tungsten baskets in order to prevent chromium coating onto the piece of gold. If evaporation is conducted in the absence of the aluminium foil block, chromium vapours will fly all over the vacuum chamber and deposit on every cold surface, including the piece of gold. The pre-treated base wafers were placed on the base plate and the system was closed using a bell jar.

![Diagram of applied current for evaporation deposition of Cr and Au on Si.](image)

Figure 3.1. Diagram of applied current for evaporation deposition of Cr and Au on Si.

Current was applied when the vacuum chamber reached the set pressure (below 10⁻⁷ bar). Firstly, chromium needs to be deposited on the surface of silicon wafers unless the base wafers are glass, quartz or mica. It was considered that the temperature of the basket reaches just over the melting point of chromium will give slow melting of a piece of chromium and therefore surfaces of the base wafers are uniformly coated with thin chromium film. In Figure 3.1 chromium was not evaporated at 10 A and 15 A applied for 15 s and 75 s, respectively although the piece of chromium glowed so strongly at 15 A that melting and evaporation appeared to occur. The two phases of liquid and solid chromium
might have been present at 15 A. When 20 A was applied, evaporation occurred and was completed within 10 s. Surfaces inside of the vacuum chamber were nicely darkened with chromium. Due to the high melting point of chromium, relatively high current (20 A) was applied for complete evaporation.

Secondly, the gold began to melt at 10 A and evaporated at 16 A. Phase-transformation from solid to liquid required about 20 s in the melt state. When the gold appeared to be almost melted, evaporation commenced for 40 s at 16 A. This process of gold deposition was repeated once more in order to optimise conditions of the deposited gold film in terms of smoothening and uniformity. Thin gold films were nicely coated all over the vacuum chamber. The thickness of gold was approximately 200 nm measured by DektakXT (BRUKER). Thickness of gold depends on volume of a vacuum chamber and the amount of evaporated gold.

Gold tends to immediately trap any organic atoms and molecules from the air, such as C, O and N, and over time more impurities are detected on the surface of gold. Therefore, exposure time of gold substrates to the air should be minimised. As soon as the vacuum chamber was opened, the substrates were cleaned by N\textsubscript{2} blow, transferred to a petri dishes or vials and thoroughly sealed. Although this process was conducted very quickly, organic impurities were found on the surfaces.

The bell jar coated with chromium and gold needs to be cleaned with gold and chromium etchant solutions. Gold etchant solution was prepared by adding 7.0 g of I\textsubscript{2} (chips, e.g., 99%+, Sigma 376558) to 22.5 g of KI (e.g., 99%+ Sigma 207969) in MilliQ water (100 mL) with stirring. This stock solution aggressively etches Au films. It is usually used at a 5:1 dilution in ultrapure water for etch rates ~200 nm/min at room temperature. Chromium etchant solution was prepared by adding 33 g of Ceric ammonium nitrate ((NH\textsubscript{4})\textsubscript{2}Ce(NO\textsubscript{3})\textsubscript{6}, 98.5%+, e.g. Sigma 215473) to 8.6 mL of HClO\textsubscript{4} (14.3 g, perchloric acid, 70%, e.g. Sigma 311421) in MilliQ water (150 mL) with stirring and the total volume was brought to 200 mL with MilliQ water.

3.1.1.3 Annealing

In micro-scale a surface of the deposited gold looks a lot of islands although the each terrace of those islands must be atomically smooth (Figure 3.2). However, their sizes are too small for the tiles and linkers to form molecular Penrose tiling, according to the size calculation above. The largest terrace is
less than 30 nm across which is barely enough for the small tiles (minimum requirement is 10 nm × 10 nm).

Annealing is the best technique to generate larger terraces of gold. In this project flame annealing and furnace annealing were carried out. Gold on glass cannot be annealed using a furnace due to its low melting point. Firstly, flame annealing procedure provided by a gold substrate supplier was used. Natural gas was used instead of hydrogen gas as a trial. A couple of attempts were unsuccessful. The gold substrates were either over-heated or under-heated. More importantly, safety was the major drawback. Handling such a small substrate and controlling flame required sufficient experience. It was also quite hard to stop heating at the end-point to avoid overheating.

The other method, furnace annealing, encountered another problem which was chromium diffusion through or into the gold layer. Heating temperature and time were varied (500 °C for 10 s, 500 °C for 10 min and 800 °C for 10 s). These resulted in the same outcome: either no annealing or diffused chromium to form chromium oxide on surfaces. This phenomenon is due to the larger diffusion coefficient of chromium than that of gold by about 105 times at 300 °C. However, furnace annealing improved the smoothness of the surfaces. Mean roughness in a region of 500 nm × 500 nm of a non-annealed sample was around 4.00 nm whereas that of a post-annealed sample by a furnace was around 1.80 nm (Figure 3.3).
<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Annealing</th>
<th>Mean roughness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Au/Si</td>
<td>No</td>
<td>4.387 nm in 1 µm × 1 µm</td>
</tr>
<tr>
<td>2</td>
<td>Au/Si</td>
<td>Furnace 500 °C for 5 min</td>
<td>1.609 nm in 0.5 µm × 0.5 µm</td>
</tr>
<tr>
<td>3</td>
<td>Au/Si</td>
<td>Furnace 300 °C for 60 min</td>
<td>0.882 nm in 0.1 µm × 0.1 µm</td>
</tr>
<tr>
<td>4</td>
<td>Au/Si</td>
<td>Furnace 500 °C for 30 min</td>
<td>0.870 nm in 0.1 µm × 0.1 µm</td>
</tr>
<tr>
<td>5</td>
<td>Au/Si</td>
<td>Furnace 800 °C for 10 s × 2</td>
<td>0.723 nm in 0.1 µm × 0.1 µm</td>
</tr>
</tbody>
</table>

Table 3.1. Annealing conditions for Au/Si substrates and its mean roughness.

Based on the results of the previous attempts, at this stage it was concluded that furnace annealing improved smoothening, although chromium diffusion was problematic. Therefore, another trial was attempted with no adhesion layer. As anticipated, the gold on silicon products got damaged so easily that holding with a tweezer could peel off the gold film and silicon appeared through the scratches. However, annealing was still carried out and resulted in significant improvement in smoothness (Table 3.1 and Figure 3.3).

![AFM images of Au/Si substrates](image1.png)

Figure 3.3. AFM images of Au/Si substrates.

### 3.1.1.4 Cleaning/recycling

Organic contaminants can be removed by piranha solution bath and oxygen plasma, which are the same procedure described in 3.1.1.1 (Pre-treatment). During the cleaning process, especially using piranha solution, too much scratched gold film may get partially and/or entirely peeled off. Additional
cleaning for STM imaging is Ar⁺ sputtering in UHV (Ultra High Vacuum) and subsequent annealing which remove minor impurities remaining on surfaces and reconstruct Au(111) surfaces. As a result, ‘herringbone’ patterns of Au(111) can be observed (Figure 3.4).

![Herringbone reconstruction of Au(111) surfaces](image)

Figure 3.4. Herringbone reconstruction of Au(111) surfaces (reproduced from ref. 91).

### 3.1.2 Characterisation

#### 3.1.2.1 X-ray Photoelectron Spectroscopy, XPS

Over time organic contaminants are gradually deposited on Au surfaces. Analysis that measures elemental composition of the surface needs to be carried out straight after the production and/or annealing. XPS is a surface-sensitive and quantitative spectroscopic technique. Empirical formula, chemical state and electronic state of the elements present in the material of surfaces can be obtained from XPS analysis.

The XPS data were collected on a Kratos Axis UltraDLD equipped with a hemispherical electron energy analyser. Spectra were excited using monochromatic Al Kα X-rays (1486.69 eV) with the X-ray source operating at 150 W. This instrument illuminates a large area on the surface and then using hybrid magnetic and electrostatic lenses collects photoelectrons from a desired location on the surface. In this case the analysis area was a 300 by 700 micron spot (=hybrid/slot). Hybrid/slot refers to the lens system in the XPS that gets the electrons from the sample surface to the analyser entrance. Hybrid means that the combination lens system was used which uses both electrostatic grids to produce electric
lensing and a magnetic snorkel lens giving magnetic lensing and hence the hybrid (electric plus magnetic) lens. The slot is an aperture within the lens column. Together these define the analysed area on the specimen. The measurements were carried out in a normal emission geometry. A charge neutralisation system was used to alleviate sample charge buildup, resulting in a shift of approximately 3 eV to lower binding energy. Survey scans were collected with a 160 eV pass energy, whilst core level scans were collected with a pass energy of 20 eV. The analysis chamber was at pressures in the 10⁻⁹ torr range throughout the data collection.

Data analysis was performed using CasaXPS. Shirley backgrounds were used in the peak fitting. Quantification of survey scans utilised relative sensitivity factors supplied with the instrument. Core level data were fitted using Gaussian-Lorentzian peaks (30% Lorentzian). The binding energy scale was corrected for the neutraliser shift by using the C 1s signal from saturated hydrocarbon at 285.0 eV as an internal standard.

All XPS analyses in this project were carried out straight after the each process to minimise exposure time of the gold samples to the air. Three to five spots of each sample were analysed and averaged. The main aim of the XPS analyses was to monitor a composition of the surface materials and determine when contamination occurred for each process. The information depth is around 2 - 3 nm.
Figure 3.5 shows XPS spectrum of non-annealed Au/Cr/Si. The composition is 66.32 - 73.69% of Au, 24.57 - 30.74% of C and 0.48 - 3.07% of O. As anticipated, the contaminants, carbon and oxygen, were observed. This indicates that deposition of these contaminants occurs immediately after exposure to the air. To avoid the contamination the substrates should either be stored and processed further in air-free system or cleaned by Ar⁺ sputtering and annealing in ultrahigh vacuum system before deposition if the substrates have already been contaminated.

An Auger electron is the second ejected electron by an electron from a higher energy level of the same atom. When a core electron is removed, an inner-shell vacancy is made. An electron from the closest or the second closest orbital falls into the vacancy and sequentially releases an electron from an outer orbital. This emitted electron from the outer orbital (lower energy level) is an Auger electron and those peaks appear in a region of higher binding energy in XPS spectra.
In the flame annealing process the Au/Cr/Si sample was overheated and therefore the deposited gold was burnt out (Figure 3.6). Oxygen was dominant (48.92%), followed by chromium (37.26%) and carbon (13.71%). Only 0.11% of Au remained and chromium oxide formed, based on the composition result. This spectrum was predicted by the appearance of the substrate which turned from gold yellow to dark grey in colour. The position of Cr 2p peak (576.99 eV) also indicates that approximately 2.5 oxygens for every Cr correspond to Cr$_2$O$_5$, according to Binding Energy Library. The binding energies of Cr, Cr$_2$O$_3$, CrO$_2$ and CrO$_3$ are 574.4 eV, 576.8 eV, 576.3 eV and 578.3 eV, respectively.

The sloped baseline is due to chromium diffusion and chromium oxide that formed on the surface. Traditionally, peak intensities are used for XPS analysis. However, when concentration of multiple atoms are being measured in a certain area of a surface, limited quantitative information can be observed. This is because peak intensities of atoms, which are chromium and gold in this case, are attenuated with the distance that electrons travelled. In the overheated Au/Cr/Si sample in the flame annealing distribution of chromium in the gold layer must be random and the electrons must travel different distances in the solid layer before exiting the solid surface in comparison with the others that...
are not overheated. As a result, energy distribution of the overheated sample and the others is different. Figure 3.6 shows that energy loss of most electrons results in the peak-energy loss. Those electrons contribute to the background of inelastically scattered electrons at lower energies. Thus, the gold signals are attenuated by the overlayer of chromium oxide on gold.

![XPS spectrum of the post-annealed Au/Cr/Si sample using a furnace at 500 °C for 5 min.](image)

Figure 3.7. XPS spectrum of the post-annealed Au/Cr/Si sample using a furnace at 500 °C for 5 min.

The peaks of oxidised chromium were observed again in XPS spectra of the furnace annealed samples at 500 °C for 5 min (Figure 3.7). Chromium diffusion still occurred due to larger diffusion coefficient of chromium than gold although proportions of Cr and O were much lower than those of the flame annealed overheated sample.\(^{90}\) 18.43% of Au, 13.60% of Cr, 31.72% of O, 35.22% of C and 1.12% of N were found. The appearance of samples did not change in a centimetre scale before and after the furnace annealing but a lot of Cr diffused and oxidised was present on the surfaces. Amounts of C and N were also enriched since the annealing was conducted at an ambient condition. In addition, the slightly sloped baseline is due to the presence of chromium oxide.
Attempts to remove the chromium oxide formed on the surface using dilute HCl solution were performed. The post-annealed Au/Cr/Si samples were soaked in dilute HCl solution for a couple of hours, washed with MilliQ water several times and dried thoroughly. However, the resulting XPS spectrum in Figure 3.8 shows that chromium oxide was still present and the sample was contaminated even more with oxygen and chlorine ion. The composition of the sample was 1.31% of Au, 31.08% of Cr, 47.00% of O, 19.72% of C and 0.88% of Cl. The chlorine ion was most likely from the water washing.
Figure 3.9. XPS spectra of the homemade Au/Si sample before (top) and after (bottom) furnace annealing twice at 800 °C for 10 s.

In order to avoid chromium diffusion during an annealing process, gold on silicon samples without the adhesion layer were prepared. It was successful that all the XPS spectra of the non- and post-annealed samples by furnace at 300 °C for 1 h, 500 °C for 30 min and twice at 800 °C for 10 s were almost identical without significant contaminations such as defused Cr (Figure 3.9). The only difference between the non- and post-annealed samples was the composition (Table 3.2). As proportions of C and
O increased, proportions of Au and I decreased after the annealing. Since the annealing was carried out at an ambient manner, more C and O were deposited on the surface. Iodine ion was found in both spectra. This represents that the gold substrate was contaminated with iodine ion before annealing, maybe from the container or the use tweezers.

<table>
<thead>
<tr>
<th>Name</th>
<th>At% before</th>
<th>At% after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 4f</td>
<td>63.70</td>
<td>55.40</td>
</tr>
<tr>
<td>C 1s</td>
<td>30.23</td>
<td>32.43</td>
</tr>
<tr>
<td>O 1s</td>
<td>5.19</td>
<td>11.34</td>
</tr>
<tr>
<td>I 3d</td>
<td>0.88</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Table 3.2. Atom compositions for the homemade Au/Si sample before and after furnace annealing twice at 800 °C for 10 s.

3.1.2.2 X-ray Powder Diffraction, XRD

XRD is a rapid analytical technique that is primarily used for phase identification of a crystalline material, based on constructive interference between monochromatic X-rays and a crystalline material. In this project XRD was used to determine single- or poly-crystallinity and quantitative composition of a sample. The instrument used in this project was SIEMENS D5000: Two-circle diffractometer using Cu Ka radiation. The angle of 2θ was scanned from 20° to 100° with a scan rate of 0.02°/s.
As shown in Figure 3.10, in the XRD result of Au/Cr/Si sample without annealing (top) Au reflections (111), (200), (220), (311), (222) and (400) were observed. A peak of Au(111) was much higher than the others. The presence of Au(222) was probably due to the same reflection from Au(111). The similar overall pattern was also observed in the XRD result of Au/Cr/glass sample without annealing. That is, thermal evaporation of Au on a Cr adhesion layer in high vacuum can only produce polycrystalline samples of Au.
The XRD result of Au/Cr/Si sample annealed by furnace at 500 °C for 10 s in Figure 3.10 (bottom) shows slight changes in decreases of Au(200), (220), (311) and (400) reflections and increases of Au(222) and Si(111). A peak of Si(111) reflection is most likely from scratches. These intensity changes of Au reflection peaks imply that annealing process re-ordered crystallinity of Au in the (111) direction, as reported.94

Figure 3.11. XRD patterns of Au/Si before (top) and after annealing by a furnace twice at 800 °C for 10 s (bottom).
Figure 3.11 shows that the XRD results of both non- and post-annealed Au/Si samples also contain reflection peaks other than Au(111) and (222) although a peak of Au(400) was not observed. However, in the top spectrum of Au/Si sample without annealing the intensities of (200), (220) and (311) peaks were much weaker than those in the XRD result of Au/Cr/Si sample without annealing (top) in Figure 3.10. Furthermore, after the annealing process using a furnace twice at 800 °C for 10 s, significant decreases in intensities of (200), (220) and (311) peaks resulted in the absence of (220) and the presence of trace amount of (200) and (311). It proves that crystallinity of the base wafer, Si(111), leads to the orientation of deposited Au in the same crystalline direction of (111). Due to no adhesion layer, strong peaks in the spectrum (top) and even stronger peaks of Si(111) in the spectrum (bottom) were observed. This increase in intensity of Si(111) peaks resulted from more scratches easily made during processes in comparison with those in the XRD spectra of no- and post-annealed Au/Cr/Si samples in Figure 3.10.

### 3.1.2.3 Electron Backscatter Diffraction, EBSD

EBSD is a surface-sensitive and SEM based technique that measure crystal orientations. The electron beam (voltages: 10 to 30 kV and currents: 1 to 15 nA) is diffracted by the crystal lattice of the specimen at the incident beam point on the specimen surface. A highly polished specimen tilted at around 70° is arranged to the incident electron beam. An Electron Backscatter Diffraction Pattern (EBSP) emanating spherically in all direction is analysed and defined by the lattice parameters of the particular crystal under the beam and by its orientation in space.

The instrument used in this project was FEI ESEM - FEI Quanta 200 F (FEG = Field Emission Gun) manufactured in the USA and EDS Detector- SiLi (Lithium drifted) with a Super Ultra Thin Window with attachments (EBSD Detector, Peltier stage (2 °C – 50 °C) and High temp stage (70 °C – 1400 °C).
The EBSD analysis of the non-annealed Au/Cr/Si sample was performed in vacuum (7.1 e⁻⁶ torr) with ETD (detector type), 1.3 e⁻⁹ torr of gun pressure and 248 µA of emission current. EBSD maps were recorded using a 20.0 keV excitation voltage, a 5000× magnification, and a 76.2° specimen tilt. Each map was acquired in hexagonal grid of scan mode with 0.05 µm step size and 9342 of number of points.

As shown in Figure 3.12 (right), the diverse crystallinities of gold were randomly distributed over the surface rather than some groups of the same crystalline directions located in an ordered pattern. This EBSD result corresponded to the XRD results where different crystallinities of (111), (200), (220), (311), (222) and (400) were observed. Figure 3.12 (left) shows that the surface of the sample was well-focused with a support of the foreign particle in the centre.

3.1.2.4 Atomic Force Microscopy, AFM

AFM is a very high-resolution type of scanning probe microscopies. A nearly atomically sharp tip (probe) attached to a cantilever is brought very close to a surface. The sharp tip interacts with the surface causing the cantilever to deflect. A simple topographic image of the surface is built up as the deflection of the cantilever is measured. Primary modes of imaging are contact mode, non-contact mode and intermittent mode (tapping). The dominant forces measured for topographic mapping are repulsive van der Waals forces for contact mode and attractive van der Waals forces for non-contact mode. By maintaining a constant oscillation amplitude a constant tip-sample interaction is maintained.
and an image of the surface is obtained. AFM was the most powerful tool to check the smoothness of homemade gold samples in this project.

AFM examinations were performed in ambient air with a commercial microscope (Dimension 3100 controlled by a Nanoscope IIIa controller, Digital Instruments, Santa Barbara, CA, USA), in the Contact-Mode, using standard unmodified silicon cantilevers (Budget Sensors, Bulgaria) with a 7-nm radius of curvature and a 42 N m\(^{-1}\) spring constant (nominal values). Topographic images were recorded at a scanning rate of 1 – 2 Hz, and a resonance frequency of about 300 kHz (nominal value). The background slope was resolved using first-order polynomial function. No further filtering was performed. Roughness values presented are averaged values obtained from three different measurements on 0.5 µm × 0.5 µm images.

Evaporation of gold on any base wafers gave flat gold films composed of small grains. Figure 3.13 shows AFM images of non-annealed Au/Cr/Si, Au/Cr/glass, Au/Cr/quartz and Au/Si samples with a range of mean roughness from 4 to 5 nm in 1 µm × 1 µm. These morphologies shown in Figure 3.13a - d are typical characteristics of gold films.\(^9\) Although Si(111) crystalline surface of the Au/Si sample helped to produce relatively larger terraces of gold in Figure 3.13d, the size of the terraces were still insufficient to allow the tiles and linkers to self-assemble in Penrose tiling which requires 100 nm x 100 nm of an atomically smooth surface as mentioned above. Moreover, terraces of the other samples which contain the chromium adhesion layer were even smaller. Therefore, annealing was a necessary step.

![AFM images](image1.png)

Figure 3.13. AFM images of non-annealed a) Au/Cr/Si, b) Au/Cr/glass, c) Au/Cr/quartz and d) Au/Si samples in 1 µm × 1 µm.

Firstly, flame annealing using the technique provided by a substrate supplier\(^8\) with natural gas instead of hydrogen gas was carried out. Loss of gold and oxidation of chromium in the overheated sample generated extremely rough surfaces in the resulting AFM images, as shown in Figure 3.14, compared
to surfaces of the non-annealed samples. The mean roughness of the overheated sample was from 15 to 20 nm, which is about 5 times larger than those of the non-annealed samples. Figure 3.14a shows the same shape of terraces appeared and overlapped. This repetitive pattern is obviously artefacts, which were probably due to the too rough surface and my lack of operating skills for AFM.

Figure 3.14. AFM images of flame annealed Au/Cr/Si samples.
Some gold still remained in small areas on the surface which were scanned by AFM, shown in Figure 3.14c and Figure 3.14d. Large islands of gold with about 100 nm in diameter were observed. Its mean roughness was between 6 nm and 7 nm. Optimisation of the flame annealing condition and reproducibility of large gold terraces would be the major issue for this flame annealing.

Another attempt to anneal samples using the flame technique without overheating appeared to be successful. Figure 3.14e and Figure 3.14f show much larger terraces of gold and improvement in smoothness. However, its mean roughness was the same range (between 2 and 4 nm) as those of the non-annealed samples. This time, I focused too much on avoiding overheating and therefore the gold film was insufficiently heated and annealing was not completed. It was concluded that a lot of practice in flame annealing and characterisations was required.

![No annealed 1 µm × 1 µm](image1)

![Annealed at 500 °C 10 s 1 µm × 1 µm](image2)

Figure 3.15. AFM images of Au/Cr/Si samples a) before and b) after annealing at 500 °C for 10 s.

Secondly, furnace annealing was the other technique which could easily control heating temperature and time. This benefit helped to avoid over-heating and under-heating which were observed on the flame annealed samples. After annealing with gradually increasing temperature from room temperature to 500 °C, merging of the gold grains on the film that would give larger terraces occurred in the AFM images, compared to the non-annealed Au/Cr/Si sample (Figure 3.15). However, the mean roughness of the Au/Cr/Si samples lowered from 2 - 4 nm to 1.6 - 1.8 nm, which was unsatisfactory. In addition, heating the Au/Cr/Si samples with gradually increasing temperature from room temperature to 800 °C evaporated the gold film, resulting in a grey surface that corresponded to the overheated sample’s surface.
a) Before annealing 1 µm × 1 µm

b) 500 °C for 5 min, 1 µm × 1 µm

c) 300 °C for 1 h, 100 nm × 100 nm

d) 500 °C for 30 min, 100 nm × 100 nm

e) 800 °C for 10 s × 2, 100 nm × 100 nm

f) 800 °C for 10 s × 2, 50 nm × 50 nm

Figure 3.16. AFM images of Au/Si samples before and after annealing.
Since the furnace annealing showed improvement in smoothness of the gold surfaces, Au/Si samples were annealed using furnace with various temperatures and heating time. Although no adhesion layer created the handling difficulty, the contamination of chromium oxide forming on the gold surface was no longer problematic. Figure 3.16 shows AFM images of Au/Si samples a) before annealing in 1 µm × 1 µm and annealed at b) 500 °C for 5 min in 1 µm × 1 µm, c) 300 °C for 1 h in 100 nm × 100 nm, d) 500 °C for 30 min in 100 nm × 100 nm, e) twice at 800 °C for 10 s in 100 nm × 100 nm and f) twice at 800 °C for 10 s in 50 nm × 50 nm. It is obvious that the gold surfaces in the AFM images were smooth with a lot of the merged grains of gold by annealing. Mean roughnesses of the samples in Figure 3.16 a), b), c), d), e) and f) were approximately 5.3 nm, 1.6 nm, 0.9 nm, 0.8 nm, 0.7 nm and 0.6 nm, respectively. Mean roughness of the post-annealed samples significantly decreased from about 5 nm to less than 2 nm. In particular, the sample with 0.6 nm of mean roughness was quite comparable with purchasable Au(111) substrates which are also 0.6 nm in mean roughness. Despite the gold films having been significantly smoothed, it was still unsuccessful that the terrace sizes of gold did not meet the calculated minimum requirement, which is 100 nm × 100 nm.

**3.1.3 Conclusion**

Gold substrates were produced using a thermal evaporation technique on silicon, glass or quartz with a chromium adhesion layer. The major crystal of Au(111) with a small mixture of (200), (220), (311) and (400) was randomly distributed, according to the XRD and EBSD results. Some organic contaminants, such as C and O, were found on the gold surfaces by XPS. The morphology of the evaporated gold film in nano-scale scanned by AFM exhibits small grains of gold with atomically flat terraces which were insufficient for molecular Penrose tiling in size.

Annealing which was performed on the Au/Cr/Si samples by flame and furnace rendered dramatic changes in smoothness and composition of gold films confirmed by AFM and XPS, but no change in crystal orientation confirmed by XRD. In both cases Cr from the adhesion layer was diffused and oxidised on the gold surfaces, according to the resulting XPS spectra. XRD still found the presence of a trace amount of crystals other than Au(111). The roughness decreased after both flame and furnace annealing. However, flame annealing was too hard to achieve to the completion due to difficulties in controlling the temperature and heating time. Only overheated or insufficiently annealed samples were produced. In contrast to flame annealing, furnace was much easier to handle.
In order to avoid Cr diffusion, Au/Si was prepared and annealed by furnace. As expected, no metal contaminants were found by XPS but still some organic contaminants were present. Proportion of crystals other than Au(111) was less than any other samples produced in this project. More importantly, furnace annealing twice at 800 °C for 10 s gave relatively flat gold substrates with 0.6 nm of mean roughness which was comparable with mean roughness of purchasable gold substrates. However, due to no adhesion layer, handling of the Au/Si samples was problematic, causing scratches which were made too easily.

Alternatively, gold on mica or gold on quartz would be a better pathway to produce atomically smooth surfaces of gold when prepared by thermal evaporation technique. Gold can adhere on mica or quartz without any adhesion layer and therefore this system can avoid diffusion of an adhesion layer during furnace annealing. Moreover, gold sputtering technique for deposition on silicon with an adhesion layer does not require any further treatment such as annealing due to the face that sputtered gold is atomically flat. Unfortunately, gold sputtering facilities were unavailable in the department.

3.2 Highly Ordered Pyrolytic Graphite, HOPG

HOPG (Figure 3.17) is one of the most commonly used substrates that has a renewable and atomically smooth surface. Unlike mica, HOPG is completely non-polar and provides a background with only carbon in the elemental signature. Like mica, HOPG consists of a lamellar structure that has much stronger forces within the lateral planes than between the planes. This can explain the characteristic cleaving properties of graphite. Based on its good conductivity, HOPG is used for STM calibration and is a good substrate for other STM samples. Its thermal stability is so excellent that the structure remains at the temperatures up to 500 °C in the air, 2500 °C in vacuum at 0.1 torr and 3500 °C in the inert atmosphere. This commercially available substrate was purchased and used for liquid-phase STM studies in this project.96
Figure 3.17. STM image of HOPG (reproduced from ref. 96).
Chapter 4  Surface deposition studies

Three types of deposition techniques for molecular surfaces that have been widely and commonly used are thermal evaporation in UHV, liquid-phase spray deposition in UHV and liquid-phase dropping technique. First of all, thermal evaporation technique has been used for depositing fullerene and pentacene on quasicrystalline-templated substrates to successfully generate monolayers of molecular Penrose tiling. Secondly, a solution of ferrocene carboxylate in benzene has been pulse-sprayed onto Au(111) and some fragments of Penrose tiling consisted of the ferrocene motifs have been observed by STM. Lastly, one droplet of aryl-triazoles in octanoic acid has been applied to a HOPG surface and their self-assembled monolayers have been investigated at the solution-solid interface by STM.

In this project the synthesised 5-fold symmetric molecules were deposited by liquid-phase dropping, liquid-phase immersing and thermal evaporation methods. The liquid-phase dropping method involves introducing a small amount of a sample solution to a surface. Deposited layers can be investigated in UHV after the droplet is dried. In addition, before evaporation of the solvent of the droplet, liquid-phase STM studies can be carried out in collaboration with Amar Flood’s group at Indiana University. The liquid-phase immersing technique, which is not a common deposition method, is to immerse a substrate into a sample solution for a certain amount of time. Once removed, the substrate is dried with N₂ blow and inserted into UHV-STM. Thermal evaporation is a deposition method in which sample molecules are evaporated by heating in UHV and deposited onto a preheated quasicrystal-template substrate to produce a monolayer. This is being studied in collaboration with Ronan McGrath at The University of Liverpool. Liquid-phase spray deposition in UHV was not carried out due to difficulties in control of production of monolayers rather than multilayers.

4.1 Liquid-phase deposition of Cam-1 on Au(111)

A preliminary deposition study for Cam-1 on Au(111) as a model was conducted to test its compatibility with the gold substrate and to optimise deposition conditions for the actual 5*, 3* and 2* tiles. Initially, the major focus of this model was to check the affinity of Cam-1 for gold which should be strong enough for deposition but not too strong for self-correction. In addition, the molecule should be deposited “flat” on a surface. Methanol was used as a solvent for this study since Cam-1 can be fully dissolved in methanol. Dichloromethane was also used although even a large volume of
dichloromethane cannot completely dissolve **Cam-1**, causing difficulties in preparation of the solutions in a different range of concentrations.

![Optimised structure of Cam-1](image)

**Figure 4.1.** Optimised structure of **Cam-1** (B3LYP/6-31G*) in a) top-view and b) side-view by GaussView5. The measured distance between the selected atoms highlighted in sky-blue. Grey: C, blue: N, red: O and white: H.

Based on calculations conducted by the Gaussian 03’ package (B3LYP and 6-31G*) assumed to occur in the gas phase at 298.15 K and 1.00 atm, **Cam-1** is 2.01 nm in diameter and 0.43 nm in height as shown in Figure 4.1. The longest distances between two protons on tert-butyl groups opposite to one another as the diameter and between two protons on one tert-butyl group as the height were measured, highlighted in sky-blue in Figure 4.1. If **Cam-1** aggregates as a dimer, the height of the dimer will become approximately 1 nm.
The two deposition methodologies applied to this study were dropping the solution onto a substrate and immersing a gold substrate into the solution. In the case of the dropping method the deposited substrates were completely dried under vacuum to ensure that Cam-1 was present on surfaces and investigate its deposition status whether “flat” or “edge-on” to the substrate. The concentration of the solution of Cam-1 was the first parameter that needed to be considered for both the dropping and immersion methods. For the immersion method exposure time of the gold substrate to the solution is another important parameter to be optimised.

4.1.1 Ellipsometry

Ellipsometry measures a change in polarization based upon reflection or transmission of light from a material structure and these reflection or transmission is usually compared to a model from the refractive index library. The measured response depends on optical properties and thickness of individual materials. In this study, ellipsometry was primarily used to measure the film thickness of Cam-1 before STM and AFM study was conducted in order to examine affinity of Cam-1 to Au(111) against glass from a vial in the case of liquid-immersion deposition method.

![Image](image_url)

Figure 4.2. Immersing deposition of Cam-1 in ‘flat’ (left) and ‘tilted’ (right) types.

Pre-cleaned homemade gold substrates with H₂SO₄/H₂O₂ (30%) mixture (3:1, v/v) followed by rinsing with water and drying with N₂ blow were placed in 20 mL or 4 mL vials. As shown in Figure 4.2, gold substrates in 20 mL vials were ‘flat’ whereas a 4 mL vial was small for the homemade gold substrate which was therefore incubated ‘tilted’. 3 mL, 5 mL or 10 mL of 5 µM solutions of Cam-1 in dichloromethane were added into the vials containing the homemade gold substrates. The solutions in the vials were allowed to evaporate open-air until dryness.
Ellipsometric thickness of the organic films were measured using a Beaglehole Imaging Ellipsometer (Beaglehole Instruments, NZ) equipped with a red LED (530 nm) using optical constants of $n = 4.1437$ and $k = 0.010521$ for Si, $n = 0.43630$ and $k = 2.2130$ for Au, $n = 1.560$ and $k = 0$ for polycarbonate and $n = 1.600$ and $k = 0$ for polystyrene. Angles of incidence were 75°, 50° and 30°. Polycarbonate and polystyrene were used as models for an organic layer as no database for Cam-1 or similar organic films was available. Gold thickness of each of bare substrate was measured to compare it with the corresponding gold thickness of deposited substrate. To minimise the ambiguity of resolving the thickness of the organic and gold layers, calculation of the thickness of the organic and gold layers for substrates after the deposition was carried out without organic layer, with polycarbonate and with polystyrene. Moreover, three or four spots on each substrate were measured to test film uniformity and to minimise variation.

Based on Appendix 1, a significant decrease in gold layers after the deposition of Cam-1 by approximately 1 nm was observed in all samples and all calculations with/without the polymer models. With regards to the Cam-1 deposited sample calculated without any organic film model, the decrease of thickness of gold layer was due to less reflection associated with the organic films of Cam-1 which were approximately 2 nm on average. However, gold thickness of the Cam-1 deposited sample calculated with the organic film models was also reduced by approximately 1 nm on average. This was probably due to the difference between Cam-1 film and polycarbonate and polystyrene in terms of their refractive index. Rough surface of gold film and some scratches on the surfaces also contributed to loss of reflection.

Nevertheless, approximately 2 nm of organic films on average were detected after the deposition. This indicated that affinity of Cam-1 to gold was much higher than glass and therefore immersing deposition technique could be applied to Cam-1 and presumably to the other campestarenes. Based on the measured data, no difference between ‘flat’ and ‘tilt’ deposition methods as well as 3 mL, 5 mL and 10 mL samples was observed in terms of thickness of the organic layers and decrease of gold thickness. This may represent a huge error in this measurement although Mean Squared Error (MSE) mostly from 0.001 to 0.003 indicated that measured data matched its model data quite well.
4.1.2 STM and AFM

Figure 4.3. STM topography images of bare Au(111) on mica a) in 2 µm × 2 µm and b) its depth profile of the red circle, c) in 200 nm × 200 nm, and d) the herringbone structure of gold pointed between 2 herringbones in 60 nm × 60 nm and e) its depth profile between herringbones.
With assistance from Dr. Haifeng Ma at The University of Canterbury and the MacDiarmid Institute, a high resolution STM and AFM study for **Cam-1** was carried out. The substrates used in this study were epitaxially grown Au(111) films on mica without annealing which were purchased from SPI Supplies (Item No: 466PS-AB). STM and AFM imaging was undertaken in a UHV chamber with a background pressure below $7 \times 10^{-10}$ mbar using a variable temperature AFM/STM (Omicron VT-AFM XA). STM scanning parameters were set to 5 pA for the tunnelling current and 1 – 2 V for the tunnelling voltage. All AFM/STM images were obtained using Pt–Ir tips.

Prior to the deposition of **Cam-1**, the purchased bare Au(111) film on mica was imaged by STM without Ar$^+$ sputtering or annealing (Figure 4.3). A lot of gold islands were observed on the surface with about 10 nm depth difference in 1 µm × 1 µm. Herringbone structure of Au(111) was also observed in about 60 nm × 60 nm and even 200 nm × 200 nm with approximately 0.1 nm depth difference although it was not as clear as Ar$^+$ sputtered and annealed ones. Roughly 100 nm × 100 nm of the terrace in average size was sufficiently large to observe extended ordering of a monolayer of **Cam-1**.
Figure 4.4. a) A photograph of the camera view of the substrate and STM topography images of Cam-1 deposited by liquid-phase dropping technique b) on the droplet ring, d) out of the droplet ring, c) and e) their corresponding depth profiles of the red circle.

Firstly, one droplet of 0.1 µM solution of Cam-1 in methanol was applied to the gold on mica substrate and the droplet was allowed to air-dry within 5 minutes. The droplet ring could be observed by the camera inside STM and thus spots in and out of the droplet ring were investigated. Approximately 2.5 nm thick multilayer of Cam-1 was observed on the droplet ring as shown in Figure 4.4b and Figure 4.4c whereas STM topography images of out of the droplet ring (Figure 4.4d) was identical to the bare gold images in Figure 4.3b and in its depth profile no evidence of deposition was found as expected.

To uniformly deposit Cam-1 on the surface, the liquid-phase immersing deposition method was attempted with the sample with the droplet ring. This attempt was to simultaneously test immersion time for a monolayer production as well as feasibility of removing the multilayer and retaining a monolayer. Hence, the substrate with the droplet ring was immersed into 0.1 µM solution of Cam-1 in methanol for 30 minutes and dried with N2 blow.
Instead of a layer, cluster types of **Cam-1** were observed on the gold surface out of the droplet ring which could be found in the camera view (Figure 4.5a). The average size of several clusters was measured and it was approximately 0.5 nm in height, 20 nm in length and 10 nm in width. This corresponded to approximately $10 \times 5$ molecules deposited ‘flat’ in line without any dimer formation. If **Cam-1** was deposited ‘edge-on’ rather than ‘flat’, the height could be larger than 1 nm. Based on the $^1$H NMR spectrum of **Cam-1** (Figure 2.11) which shows tendency of **Cam-1** to aggregate to dimers in solution at room temperature, unexpectedly no dimers of **Cam-1** were found on the surface. Figure 4.6 shows an example of one of the clusters of **Cam-1** monomers.
Figure 4.6. STM topography images of **Cam-1** deposited by liquid-phase immersing technique for out of the droplet ring in 200 nm × 200 nm (top) and their depth profiles of the red circles (bottom): width-right, legth-middle and width of another sample-right.

As shown in Figure 4.7, on the droplet after the washing step by liquid-phase immersing method multilayer still remained on the upper terraces of the gold film whereas some flower-like clusters were observed on the lower terraces. Size of the flower-like clusters was approximately 8 nm in diameter and 0.4 or 0.8 nm in height. This indicated that monomers and dimers were present at ambient condition in contrast to the STM topography images from the upper terraces (Figure 4.6) which showed monomers only. However, those flower-like clusters appeared to be so repetitive that they were most likely artefacts.
Another attempt of liquid-phase immersing deposition was carried out with a bare gold on mica substrate in 0.05 µM solution of Cam-1 in methanol for 60 minutes. Before inserting the substrate into UHV-STM, the gold surface was dried with N₂ blow. As previously observed in STM topography images above, instead of monolayers, the clusters were found on both upper terraces and lower terraces of the gold films (Figure 4.8). In particular, a few group of four clusters were found and the size of the four clusters was 0.4 nm in height (0.1 nm from the valley to the top), 5 nm × 2 in diameter. This corresponded to four Cam-1 molecules in a group of four clusters.
Figure 4.8. a) A photograph of the camera view of the substrate and STM topography images of Cam-1 deposited by liquid-phase immersing technique (0.05 µM in methanol for 60 min) in b) 500 nm × 500 nm, c) 200 nm × 200 nm, d) 150 nm × 150 nm and e) its depth profiles of the red circle.

Often, the Pt–Ir tips are contaminated with atoms from the top layers during imaging process. Therefore, the tip that could be contaminated with organic atoms was cleaned by applying V-Pulse (V-Pulse: from -10 V to 10 V, T-Pulse < 1 ms) to the tip. When applying the voltage pulse to the tip in a short time, a large number of electrons are transferred either from the tip to the substrate or from the substrate to the tip. The exchange process results in removal of contaminants on the tip and/or change of the tip status by directly picking up atoms from the substrate. In this case, electrons were transferred from the gold substrate to the tip which might pick up some Au atoms from surface and this could improve the image resolution through Au atoms on the top of the tip. Obviously, line-type clusters were observed in STM topography images before the tip-cleaning process whereas more spots appeared and no line-type clusters were found in the STM image shown in Figure 4.9b.
In order to double-confirm the successful deposition of **Cam-1** on gold surface, AFM on non-contact mode was conducted with the current sample deposited by liquid-phase immersing method using 0.05 µM solution of **Cam-1** in methanol for 60 minutes (Figure 4.10). Spots of **Cam-1** clusters were observed on both upper and lower terraces of the gold film. The size of one of the clusters was approximately 0.6 nm in height and 10 nm in diameter. This size roughly matched the size of the clusters found in the STM topography images (Figure 4.5 and Figure 4.7).

This consistent result of **Cam-1** clusters observed by STM and AFM confirmed that **Cam-1** molecules were definitely deposited as clusters on gold surfaces instead of a monolayer. Variation of concentrations of the **Cam-1** solutions (0.1 µM and 0.05 µM in methanol) and immersion time (30 min and 60 min) which resulted in almost identical STM and AFM images were unsuccessful for optimising the deposition conditions. It was suggested that the immersing times should be at least 12 to 24 hours to obtain a decent monolayer to view its ordering.
The substrate was cleaned using Ar⁺ sputtering with 2.5 kV for 15 min and annealing at 400 °C for 30 min. As expected, herringbone reconstruction pattern of Au(111) was clearly observed on the upper terraces in 100 nm × 60 nm and even 180 nm × 180 nm as shown in Figure 4.11b and Figure 4.11c. However, it was surprising that on the lower terraces some random patterns of remaining Cam-1 were found in 180 nm × 180 nm and 130 nm × 70 nm in Figure 4.11b and Figure 4.11d. Fifteen minutes of Ar⁺ sputtering with 2.5 kV was insufficient to remove the clusters of Cam-1 and during the annealing at 400 °C the remaining molecules re-orientated in such a random order. This shows that heating can play a key role as a driving force for rearranging the tiles after deposition of a surface. In the first
deposition of the tiles in monolayers on a surface probability of 5*, 3* and 2* tiles that orientate in a long range of Penrose tiling is extremely low and correction of positions of the tiles will be essential.

Figure 4.11. STM topography images of Au(111) after cleaning by Ar⁺ sputtering with 2.5 kV for 15 min and annealing at 400 °C for 30 min in a) 500 nm × 500 nm, b) 180 nm × 180 nm, c) 100 nm × 600 nm and d) 130 nm × 70 nm.
As shown in Figure 4.12, repetitive heating and cooling in a gradual increase and decrease of heating temperature may improve the ordering of the monolayer. The maximum heating temperature should be high enough to allow the tiles to become mobile so that the tiles can move into their right position. In the meantime, too high temperature will result in loss of the tiles which may either decompose or evaporate off. Therefore, optimisation of the maximum heating temperature will be the key step for this rearranging process. Heating time at the maximum temperature also needs to be investigated.

![Figure 4.12. Hypothetical graph of repetition of heating and cooling for optimisation of the tiles rearrangement.](image)

Another important step is re-heating after cooling. Re-heating is required for remaining tiles that are not in the right position to rearrange and correct themselves to form tiling pattern. Optimisation of heating temperature is crucial so that tiles in the right positions must not be relocated but tiles in wrong positions need to become sufficiently mobile to relocate to the right position as shown in Figure 4.13b. Tiles in the right positions are fully bonded via intermolecular interaction: for example, 5*- , 3*- and 2*- tiles are bonded with 5, 3 and 2 adjacent tiles whereas tiles in wrong positions including overlapped tiles are missing at least one bonding as shown in Figure 4.13. This implies that there must be a certain temperature where tiles in wrong positions can move but tiles in the right positions cannot. Repeating process of heating and cooling (Figure 4.12) will be the best method to find the optimal temperature. In particular, the re-heating steps after cooling will minimise technical errors of controlling temperature and optimisation of heating time.
Figure 4.13. Examples of fractions of Penrose tiling with a) an overlap in red and b) possible self-correction in blue.

4.2 Liquid-phase deposition on HOPG

This work was achieved by collaboration with Professor Amar Flood and Professor Steve Tait’s groups in Indiana University and carried out by Brandon Hirsch. Scanning tunneling microscopy experiments were carried out on Agilent Technologies 5500 PicoPlus STM using a Picoscan controller in constant-current mode. Tips were mechanically cut from Pt/Ir wire (80:20, diameter 0.2 mm). The HOPG substrate (ZYB, Mikromasch) was mechanically cleaved before each experiment. A liquid cell was made from Teflon using a Viton O-ring to ensure the solution was contained over a defined area. Samples were prepared by dropping 10 μL of solution on the surface with a micropipet.

Solutions of the ethyl ester campestate (Cam-4) were prepared in a 40:60 mixture of 1,2,4-trichlorobenzene: dichloromethane across a range of concentrations (20 μM to 2 mM). The STM images of Cam-4 are from the prepared 20 μM solution. In the STM images of Cam-4 some short lamella orderings with 1.73 nm repetition of the molecules were observed (Figure 4.14 - Figure 4.16). Computational modelling was carried out using Spartan’14 and Hyperchem (8.0.10) to compare the obtained STM images with the computationally produced structures (Figure 4.17). The modelling molecular structure was built by Spartan’14 and exported into Hyperchem (8.0.10). In Hyperchem, the built molecules were arranged and compared to the measurements acquired by STM. The four molecules were translated such a way that they were placed in appropriate lattice positions as determined by the STM images. Once the molecules were located in the appropriate lattice positions, point rotations of the molecules were performed to ensure that no clear steric clashes occurred in the entire packing structure. Next, individual bond dihedrals were rotated to ensure optimal intermolecular contacts as judged by chemical intuition. The intermolecular contacts were again examined in Spartan to double-check that the resulting structure was reasonable.
The core to core distance between two Cam-4 molecules in Figure 4.17 was 2.5 nm whereas the obtained STM images showed the 1.73 nm repetition. It was suggested that the ethyls on the esters which can flexibly rotate occupied in a space between the esters and intermolecular hydrogen bonding between the oxygens on the esters and the hydrogens on the methyls brought the molecules closer. Therefore, the core to core distance has become shortened up to 1.73 nm as observed in the STM images.

Figure 4.14. STM topography (top) and current (bottom) images of the ethyl ester campestarene (Cam-4) on HOPG.
Figure 4.15. STM topography (top) and current (bottom) images of the ethyl ester campestarene (Cam-4) on HOPG.
Figure 4.16. STM topography image of the ethyl ester campestarene (Cam-4) on HOPG with the distance measurement of approximately 1.7 nm highlighted in green between the two Cam-4 molecules.

Figure 4.17. Ordering structure of Cam-4 produced by Spartan’14 and Hyperchem (8.0.10). C: skyblue, O: red, N: blue and H: white.
As shown in Figure 4.18 and Figure 4.19, the benzyloxy SP (SP-4*) and the methoxy campestarene (Cam-3) did not assemble in any orderings as their substituents did not have intermolecular interaction properties. Solutions of SP-4* and Cam-3 were prepared in 1,2,4-trichlorobenzene and water across a range of concentrations (20 μM to 5 mM), respectively. The STM images of SP-4* and Cam-3 are from the prepared 375 μM and 75 μM solution, respectively. The well-spread SP-4* molecules were observed on a surface in no-ordering in Figure 4.18 whereas mostly empty spaces and the aggregated Cam-3 molecules were observed in Figure 4.19. Pure Cam-3 is soluble only in DMF and DMSO but sodiated Cam-3 can be dissolved in water and thus water was used as a solvent for Cam-3. However, the lack of assembly from Cam-3 was the result of use of inappropriate solvent. After the aqueous solution delivery and subsequent evaporation on the surface ‘coffee ring stains’ associated with aggregation of Cam-3 were observed.
Figure 4.18. STM topography (top) and current (bottom) images of SP-4* on HOPG and its molecular structure.
Figure 4.19. STM topography (top) and current (bottom) images of **Cam-3** on HOPG and its molecular structure.
The synthesised molecules listed below are currently under investigation by STM in collaboration with Flood and Tait’s group; Croconate and its derivatives: \([\text{AgNa(C}_5\text{O}_5)(\text{H}_2\text{O})_2]_n\) (CO-1), 1,2,4-cyclopentanetrione (CO-4), 3,5-diphenylcyclopentane-1,2,4-trione (CO-7), cyclopent-4-ene-1,3-dione (CO-8), 2-methyl-1H-indene-1,3(2H)-dione (CO-9), pentacyano-cyclopentadienyl (PCN-3), 5*-campestarenes: penta-acetoxy campestarenes (Cam-5) and penta-propionicoxy campestarene (Cam-6), the butyl phenyl carboxylic acid campestarene (Cam-10) and the hepty phenyl carboxylic acid campestarene (Cam-11), 3*-campestarenes: the mixture of 3*-campestarene (Cam-13), 2*-campestarene (Cam-14) and other isomers.

4.3 Thermal evaporation deposition on quasicrystalline templates

In collaboration with McGrath’s group an investigation of thermal evaporation deposition of 5-fold symmetric molecules on quasicrystalline templates as substrates is being carried out. Since flat molecules with 5-fold symmetry have not yet been deposited by thermal evaporation on quasicrystalline templates in UHV, it will be interesting to investigate deposition conditions for flat molecules with 5-fold symmetry in comparison with fullerene and pentacene.\(^{20}\) Once a monolayer of the 5-fold symmetric molecules templated by a quasicrystal substrate is successfully produced, variety of further studies can be carried out, such as analyses of the molecular quasicrystalline layers using XPS, LEED and GI-SAXS, thermal deposition with linker-containing pentagonal molecules, production of molecular quasicrystalline multilayers, separation of the molecular quasicrystalline layers from the substrate and investigation of chemical properties of the molecular quasicrystalline layers. Therefore, the currently investigated molecules are the methoxy-Singapore Pentamer (SP-1), the fluoro-Singapore Pentamer (SP-7), penta-tert-butyl campestarene (Cam-1) and CB[5] as well as CB[6] and CB[8] for comparison.
Chapter 5  Summary and future work

5.1 Summary

A series of molecular pentagons across a range of different size of molecules including monomeric molecules, macrocycles and supramolecules has been synthesised and characterised in this project. Firstly, a set of 5*- and 2*-tiles of croconate and its derivatives has been prepared. A coordination chemistry study of croconate and squarate with cobalt indicated that the carbon-oxygen-metal bonding is not linear and croconate tends to chelate in bidentate geometry. Secondly, pentacyano-cyclopentadienide was successfully synthesised. However, syntheses of 2*- and 3*-tiles were not carried out due to the required use of the hazardous reagent cyanogen bromide. Thirdly, campestarenes substituted with a variety of functionalities have been synthesised. The substituents are tert-butyl, methoxy, bromide, acetic acid, propionic acid, pyridyl, benzonitrile, benzoic acid and alkylated benzoic acids. Campestarenes with acetic acid and propionic acid substituents (Cam-5 and Cam-6) were successfully isolated using Sephadex G-10 column chromatography, followed by acid-base washing. MALDI-MS confirmed the syntheses of bromo, pyridyl, benzonitrile, benzoic acid, and alkylated benzoic acid campestarenes were successful whereas NMR spectroscopy did not show clear signals probably due to their poor solubility as well as the biphenyl units causing aggregation via π-π stacking. The 3*- and 2*- tiles (Cam-13 and Cam-14) were also synthesised. Fourthly, the intermediate of 5*-Singapore Pentamer (SP-5*), hydroxyl Singapore Pentamer and S-25 for fluoro-Singapore Pentamer (SP-8) have been synthesised. Production of 3*- and 2*-SP (SP-9b and SP-9d) has also been attempted using a mixture of the H-precursor (S-17) and the methoxy precursor (S-18). This attempt proves that production of 3*- and 2*-tiles of SP is feasible. Lastly, cucurbit[5]uril has been successfully functionalised using aryl boronic acids via condensation. MALDI-MS confirm the presence of 5*-CBs whereas NMR spectroscopy showed signals for the unreacted aryl boronic acids which is presumably due to pH dependant reversible equilibrium property of the boron-oxygen bonds on 5*-CBs. The pathway to production of 3*- and 2*-CBs via pre-synthesis derivatisation using dimethyl glycoluril was introduced.

Preparation of gold substrates was carried out using thermal evaporation technique on silicon, quartz and glass as parent substrates. Chromium was selected as an adhesion layer since gold does not adhere directly on silicon. Annealing was essential that without annealing the gold surfaces were too rough to be used for Penrose tiling production. Furnace annealing was applicable to gold on silicon only since
the melting point of glass is too low and chromium oxides were found on the surfaces after annealing due to higher diffusion coefficient of chromium than gold. Furnace annealing achieved mean roughness of 0.6 nm of gold surfaces tested by AFM. The gold crystal uniformity was examined by XRD and EBSD that the major crystallinity was (111). Au(200), (220), (311) and (400) were also found and well distributed throughout the surfaces. Surface components were detected by XPS that gold tends to absorb carbon, oxygen and nitrogen from the air.

Preliminary deposition and characterisation studies by high-resolution STM and AFM were carried out in collaboration with Dr. Haifeng Ma at The University of Canterbury, Professor Amar Flood and Professor Steve Tait at Indiana University. Cam-1, Cam-2 and SP-4 did not assemble in an ordered fashion since their functionalities, tert-butyl, methoxy and benzyloxy do not have intermolecular binding properties. However, the ethyl ester from Cam-4 allowed Cam-4 to assemble in lamellar ordering on HOPG.

5.2 Future work

Future work can be completion of the isolation of 3*- and 2*-campestarenes, the syntheses of 5*- , 3*- and 2*-SPs, full characterisation of 5*-CB and syntheses of 3*- and 2*-CBs. All the synthesised molecular pentagons also need to be deposited on surfaces and their assemblies in monolayers should be studied using various characterisation techniques: AFM, STM, XPS, LEED, GI-SAXS and TEM (in case of link by metals). Ratio of 5*- , 3*- and 2*-tiles to each other as well as ratio of tiles to metals in case of metal linkage system should be calculated for production of long-range Penrose tilings.

Other candidates as molecular tiles are cyanostar, corannulene, pentafoil knot and metallacyclophanes. Cyanostar is a flat pentagonal molecule and synthesis of ester-terminated cyanostar has been synthesised. Corannulene is a bowl-shape molecule with 5-fold symmetry. Kilogram scale synthesis of corannulene and selective functionalization using different solvents have been reported. It might be interesting to create quasicrystals with pentafoil and metallacyclophanes although it will be synthetically challenging. If a set of 5*- , 3*- and 2*-tiles with ●-○ recognition (like DNA type) is designed for covalent organic framework (COF) type assembly, the unwanted orientation comprised of only 3*-tiles (Figure 1.16) can be avoided.
Investigation of physical properties of molecular Penrose tiling should be carried out since unusual properties of quasicrystals are observed in 3D alloys. Possible examples of applications could be a light absorber made from pentaphyrins (expanded porphyrins) for light harvesting, materials for new optoelectronic devices particularly in the THz spectral range based upon enhanced transmission resonances with line shapes,\textsuperscript{15b} and photonic band gap materials that have sufficiently high dielectric contrast to support absolute photonic gaps\textsuperscript{103} and to realise and investigate the localisation of light.\textsuperscript{104} Cucurbit[5]urils are known to have gas absorption properties.\textsuperscript{74} Quasicrystals comprised of cucurbit[5]urils which may have good physical properties such as thermal stability and long life-time could potentially be used for gas separation, gas filtration and/or gas storage.

Furthermore, it is possible that formulating the principles of 2D molecular Penrose tilings will produce 3D molecular Penrose tilings by growing on top of 2D quasicrystal layers. Growth mechanisms for decagonal quasicrystals achieved by lateral growth rule, vertical growth rule and island nucleation for seed formation has been reported.\textsuperscript{105}
Chapter 6  Experimental

General information

All reagents and solvents were obtained from commercial suppliers and used as received unless otherwise noted. All dry solvents were collected from a solvent purifier manufactured by LC Technology Solutions Inc. (www.ictechinc.com). Sephadex G-10 gel filtration columns (Amersham Bioscience) are used for the isolation and purification of products. “MilliQ” water was used in all synthetic procedures and in the preparation of Sephadex G-10 columns.

High resolution mass spectra were recorded on a Bruker microHTOFQ (Hybrid Quadropole Time of Flight) mass spectrophotometer in electrospray ionisation (ESI) mode. MALDI-TOF MS analyses were performed using saturated α-cyano-4-hydroxycinnamic acid in 30% water in methanol as matrix on a Voyager-DE™ PRO MALDI-TOF mass spectrometer (Applied Biosystems, Inc., Foster City, CA). Prior to data collection, a linear external calibration was performed using the mass calibrants: bovine insulin (Mr = 5734), Escherichia coli thioredoxin (Mr = 11,674) and equine apomyoglobin (Mr = 16,952). For presentation, acquired ESI and MALDI mass spectra underwent smoothing and baseline subtraction using mMass (Version 5.5.0).\textsuperscript{106} GC-MS analyses were carried out using Agilent Technologies 7890A GC equipped with Agilent Technologies 5975C mass detector and Restek Rxi-5ms column. Microanalyses were carried out at the Campbell Microanalytical Laboratory, The University of Otago.

\textsuperscript{1}H, \textsuperscript{11}B, \textsuperscript{13}C, \textsuperscript{19}F NMR, COSY, HSQC, HMBC and NOESY spectra were recorded on a Bruker Avance III 300, 400 or HD 500 spectrometers. Spectra recorded in CDCl\textsubscript{3}, D\textsubscript{2}O, CD\textsubscript{3}OD, and d\textsubscript{6}-DMSO were referenced to TSP-\textsubscript{d4}, or the respective residual solvent peaks. X-ray diffraction data were collected on a Siemens SMART CCD diffractometer at The University of Auckland. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 infrared spectrometer.

(NEW) denotes compounds that have not yet been reported.
Croconate

[AgNa(C₅O₅)(H₂O₂)]ₙ, CO-1₄₃a

Disodium croconate (0.093 g, 0.5 mmol) in water (2.50 mL) was added dropwise to silver nitrate (0.085 g, 0.5 mmol) in water (7.50 mL) at r.t. while excluding light. The mixture was stirred for 30 min. The solution changed from orange/yellow to green. A black precipitate was filtered off. The filtrate was allowed to crystallise slowly in a CaCl₂ desiccator. After a few days shiny yellow/green crystals were obtained. Yield: 0.134 g, 87%

The collected single crystal X-ray crystallography data corresponds to the literature values."⁴₃₄

IR: v = 3503, 3360, 2168, 1716, 1672, 1646, 1623, 1569, 1480, 1113, 725, 648, 570, 514, 407 cm⁻¹.
Cobalt squarate, \([\text{Co(C}_4\text{O}_4)(\text{H}_2\text{O})_4]_n\), CO-2\(^{49a}\)

A mixture of squaric acid (0.057 g, 0.5 mmol) and cobalt(II) acetate tetrahydrate (0.125 g, 0.5 mmol) in EtOH (15.0 mL) was stirred at r.t. for 72 h. After stirring, the colour of the solution changed from red/purple to creamy purple with a noticeable odour of acetic acid. A pink precipitate was filtered, washed with water and thoroughly dried under vacuum. Yield: 0.120 g, 98%

Single crystal X-ray crystallography was performed for characterisation. The pink solid product was dissolved in water using an ultrasonicator and stood in a CaCl\(_2\) desiccator until a single crystal formed. The collected single crystal X-ray crystallography data corresponds to the literature values\(^{49a}\).

\[\text{IR: } \nu = 3242, 1489, 1104, 746, 661 \text{ cm}^{-1}.\]
Cobalt croconate, \([\text{Co(C}_5\text{O}_3\text{(H}_2\text{O})_3]\)\text{in}, \text{CO-3}^{49b}

A pink solution of cobalt(II) acetate tetrahydrate (0.055 g, 0.1 mmol) in water (8.00 mL) was added dropwise to a yellow solution of croconic acid (0.014 g, 0.1 mmol) in water (8.00 mL). The reaction mixture was stirred at r.t. overnight. After stirring, the colour of the solution changed from yellow to orange with a noticeable odour of acetic acid. The solvent was removed under vacuum to give a dark red product. Yield: 0.025 g, 99%

Single crystal X-ray crystallography was performed for characterisation. The dark red solid product was dissolved in water using an ultrasonicator and stood in a CaCl\(_2\) desiccator until a single crystal formed. The collected single crystal X-ray crystallography data corresponds to the literature values.\(^{49b}\)

IR: \(\nu = 3450, 3273, 2257, 1674, 1503, 1459, 1326, 1111, 1034, 841, 792, 673\) cm\(^{-1}\).
A mixture of dibenzyl ketone (2.10 g, 10 mmol) and diethyl oxalate (1.50 g, 10 mmol) was added dropwise to sodium (0.460 g, 20 mmol) in dry EtOH (10.0 mL) at 0 °C with vigorous stirring. The colour of the solution changed from colourless/creamy to orange/red and then to dark purple. The reaction mixture was stirred at 0 °C for 3 h and at r.t. for 48 h. After 48 h stirring, the solution had turned black/yellow in colour. A few drops of acetic acid were added to the mixture for neutralisation until the pH reached 7 and the solution turned light/creamy yellow in colour. The reaction mixture was filtered through Celite to remove red oil and washed with water. 2 N H₂SO₄ (50.0 mL) was added dropwise to the filtrate to give a yellow precipitate which was recrystallized from xylene once and from EtOH twice. Yield: 0.766 g, 29 %

HRMS (ESI)
[M+H]⁺ 265.0866 (measured), 265.0859 m/z (calculated): C₁₇H₁₃O₃
[M+Na]⁺ 287.0679 m/z (measured), 287.0679 m/z (calculated): C₁₇H₁₂O₃Na
[M+K]⁺ 303.0420 m/z (measured), 303.0418 m/z (calculated): C₁₇H₁₂O₃K
GC-MS: 264.1 m/z (measured), 264.1 m/z (calculated): C₁₇H₁₂O₃

¹H NMR (300 MHz, CDCl₃): δ = 8.22 (dd, 2 H, ⁴J = 8.4 Hz, Ar-H), 7.51-7.44 (m, 3 H, Ar-H), 7.38-7.32 (m, 3 H, Ar-H), 7.23-7.21 (m, 2 H, Ar-H), 4.16 (s, 1 H, Ar-CH)

¹³C NMR (75 MHz, CDCl₃): δ = 196.46 (C=O), 162.53 (C-OH), 143-128 (Ar-H), 55.37 (Ar-CH)
2,4,5-Trioxo-1,3-diphenylcyclopentane-1,3-diide, CO-6

NaH (60% dispersion in mineral oil, 0.012 g, 0.3 mmol) was washed with dry n-hexane to remove the oil and suspended in dry MeCN (30.0 mL). 4-hydroxy-2,5-diphenylcyclopent-4-ene-1,3-dione, CO-7 (0.027 g, 0.1 mmol) was added to the solution at r.t. and the reaction mixture was stirred at r.t. for 1 h under Ar. The solution turned purple in colour. Removal of the solvent gave a purple oil. Yield: 0.026 g, 99%.

Note: the purple oil was exposed to air for 1-2 min and turned yellow which corresponds to 4-hydroxy-2,5-diphenylcyclopent-4-ene-1,3-dione.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.40 \text{ (dd, 2 H, } J = 1.0 \text{ Hz, Ar-}H), 6.94 \text{ (t, 2 H, } J = 7.4 \text{ Hz, Ar-}H), 6.50 \text{ (t, 1 H, } J = 7.0 \text{ Hz, Ar-}H)$

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 202.18 \text{ (C6 or C7), 183.41 (C6 or C7), 140.26 (C4), 126.59 (C2), 122.21 (C3), 116.87 (C1), 94.66 (C5)$

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2-Methyl-1H-indene-1,3(2H)-dione, **CO-9**

3-pentanone (5.28 mL, 50 mmol) was added dropwise to NaH (2.43 g, 61 mmol) suspension in dry toluene (100 mL), followed by dimethyl phthalate (8.16 mL, 50 mmol). The reaction mixture was stirred for 1 h. The reaction mixture was refluxed for 3 days and then cooled to r.t. to give a red/orange oil which solidified. The solid product was collected by filtration, washed with toluene and dried under vacuum. The crude product was redissolved in water (500 mL) and the solution was acidified with conc. HCl (5.00 mL) to give a yellow oil which was solidified after standing overnight at r.t. The yellow solid was filtered and dried under vacuum. Yield: 7.89 g, 99%.

**HRMS (ESI)**

\[ [\text{M+H}]^+ \ 161.0593 \text{ m/z (measured)}, \ 161.0524 \text{ m/z (calculated): C}_{10}\text{H}_9\text{O}_2 \]

**GC-MS**: 160.0 m/z (measured), 160.0 m/z (calculated): C\text{\_}_{10}\text{H}_8\text{O}_2

**\(^1\text{H NMR}\)** (400 MHz, CDCl\text{\_}3): \( \delta = 7.99\text{-}7.96 \text{ (m, 2 H, H5)}, 7.87\text{-}7.83 \text{ (m, 2 H, H6)}, 3.08 \text{ (q, 1 H, }^{3}J = 7.6 \text{ Hz, H2}), 1.42 \text{ (d, 3 H, }^{3}J = 7.6 \text{ Hz, H1}) \)

**\(^1\text{H NMR}\)** (400 MHz, DMSO): \( \delta = 7.96 \text{ (s, 4 H, H5,H6)}, 3.44 \text{ (q, 1 H, }^{3}J = 7.6 \text{ Hz, H2}), 1.25 \text{ (d, 3 H, }^{3}J = 7.6 \text{ Hz, H1}) \)

**\(^{13}\text{C NMR}\)** (100 MHz, DMSO): \( \delta = 200.94 \text{ (C3), 141.58 (C4), 135.85 (C6), 122.77 (C5), 48.49 (C2), 9.54 (C1)} \)
2-Methyl-1,3-dioxo-2,3-dihydro-1H-inden-2-ide, **CO-11**

![Chemical Structure](image)

NaH (60% dispersion in mineral oil, 0.006 g, 0.15 mmol) was washed with dry *n*-hexane to remove the oil and suspended in dry MeCN (50.0 mL). 2-methyl-1H-indene-1,3(2H)-dione, **CO-9** (0.016 g, 0.1 mmol) was added to the solution at r.t. and the reaction mixture was stirred at r.t. for 1 h under Ar. The solution turned from yellow/orange to orange in colour. Removal of the solvent gave an orange oil. Yield: 0.015 g, 94%.

Note: the orange oil was exposed to air for 1-2 min and turned more yellow which corresponds to 2-methyl-1H-indene-1,3(2H)-dione.

\(^1\)H NMR (400 MHz, DMSO): \(\delta = 7.07 \text{ (dd, 2 H, } ^4J = 3.0 \text{ Hz, } H5), 6.90 \text{ (dd, 2 H, } ^4J = 3.0 \text{ Hz, } H6), 1.47 \text{ (s, 3 H, } H1)\)

\(^{13}\)C NMR (100 MHz, DMSO): \(\delta = 189.06 \text{ (C3), 171.43 (C2), 141.54 (C4), 128.09 (C6), 115.45 (C5), 6.82 (C1)}\)
Pentacyanocyclopentadienide

Ethane-1,1,2,2-tetracarbonitrile, PCN-1 \(^{56d}\)

A solution of ethene-1,1,2,2-tetracarbonitrile (19.2 g, 15 mmol) in acetone (75.0 mL) was cooled to 0°C. To this yellow solution was added mercaptoacetic acid (30.0 mL, 40 mmol) with stirring and the mixture became rich yellow then faded to colourless within 10 s. Ice-cold water (150 mL) was added to the mixture at 0°C to give a pale yellow solution which stood at r.t. for 3 days to give a white/yellow precipitate. Another addition of water (300 mL) and standing for 24 h gave more precipitate which was filtered, washed with ice-cold water and dried under vacuum. The light yellow product was hygroscopic and slightly impure according to \(^1\)H NMR. Yield: 0.684 g, 35%

\(^1\)H NMR (300 MHz, DMSO): \(\delta = 4.02\ (s,\ 2\ H,\ C1H)\), \# Peaks of impurities were observed around \(\delta = 4\)

\(^{13}\)C NMR (75 MHz, DMSO): \(\delta = 33.85\ (C1),\ 174.49\ (C2)\)
1,4-Dithiine-2,3,5,6-tetracarbonitrile, PCN-255.107

[Diagram of 1,4-Dithiine-2,3,5,6-tetracarbonitrile]

Carbon disulfide (7.61 g, 0.1 mol) was added dropwise with vigorous stirring to sodium cyanide (4.90 g, 0.1 mol) in dry DMF (30.0 mL) over 1 h. As the addition time went by, the solution changed in colour from colourless, to yellow, to darker yellow and to black yellow. Stirring was continued until crystallisation occurred. The reaction mixture was then poured into a 250 mL conical flask with water. The volume was adjusted up to 250 ml and left overnight. The solution was filtered away from the deposited crystals which were elemental sulfur. Ammonium persulfate (22.9 g, 0.1 mol) in water (50.0 mL) was added dropwise to the filtrate over 1 h. A yellow/brown precipitate was observed. The mixture was stirred for 10 min and thoroughly dried under vacuum. The crude product was purified by Soxhlet extraction using carbon disulfide as a solvent for 72 h. The remaining solid in the thimble was collected and dried under vacuum. Filtration using hot toluene and recrystallization from toluene were carried out for further purification to give a yellow solid which included ca.10% of sulfur. Yield: 2.77 g, 51%

GC-MS: 215.9 m/z (measured), 215.9 m/z (calculated): C₈N₄S₂

IR: ν = 3215, 2229, 2177, 1598, 1519, 1415, 1312, 1177, 1158, 1137, 1114, 1099, 1026, 1011, 977, 626, 521, 505, 498, 482, 473, 420 cm⁻¹.

The IR spectrum corresponds to the literature values.107

¹³C NMR (75 MHz, CD₃CN): δ = 125.20 (SCCN), 112.18 (CN)
Methyl cyanoacetate (0.440 mL, 5 mmol) was added to a suspension of sodium hydride (0.400 g, 10 mmol) in dry THF (50.0 mL) at 0 °C. After H₂ evolution had ceased (about 10 min), 1,4-dithiine-2,3,5,6-tetracarbonitrile, PCN-2 (1.60 g, 5 mmol) was added at 0 °C. The reaction mixture was stirred at r.t. until H₂ evolution again ceased (about 1 h) and then refluxed for 3 h (the oil bath temp was 120 °C), cooled to r.t. and dried under vacuum. The residue was extracted with water (54.0 mL) and tetraethylammonium chloride (0.820 g, 5 mmol) was added to the extract. A yellow solid precipitated, filtered and washed with water. The dark brown crude product stuck to the sinter funnel. EtOH redissolved the crude product which was extracted from the sinter funnel and stood at r.t. until crystals formed. Yield: 0.085 g, 8%

HRMS (ESI)
[M]⁺ 190.0156 m/z (measured), 190.0159 m/z (calculated): C₁₀N₅
[M]+ 130.1592 m/z (measured), 130.1590 m/z (calculated): C₈H₂₀N

IR: ν = 3408, 3300, 2959, 2925, 2854, 2216, 1995, 1745, 1686, 1610, 1531, 1508, 1485, 1439, 1365, 1305, 1259, 1194, 1079, 1015, 799, 734, 464 cm⁻¹.

¹H NMR (300 MHz, DMSO): δ = 3.23 (q, 8 H, ³J = 7.2 Hz, Ha), 1.15 (m, 12 H, Hb)

¹³C NMR (75 MHz, DMSO): δ = 113.01 (CN), 101.72 (Cs ring), 51.34 (Ha-C), 7.05 (Hb-C)
Campestarenes

General Method A.\textsuperscript{34} Two equivalents of Et\textsubscript{3}N was added dropwise to a mixture of the corresponding phenol, 2 equivalents of MgCl\textsubscript{2} and 2.2 equivalents of paraformaldehyde in dry THF. The reaction mixture was refluxed for 24 h, cooled to r.t. and dilute HCl was added until the remaining solid was completely dissolved. The organic phase was removed by rotary evaporation and then the aqueous phase was extracted with DCM. The combined extracts were dried over MgSO\textsubscript{4}, filtered and the solvent removed under vacuum. The crude product was purified by silica gel flash column chromatography.

General Method B.\textsuperscript{109} A mixture of the corresponding phenol, 1.5 equivalents of MgCl\textsubscript{2}, 3.8 equivalents of Et\textsubscript{3}N and 5 equivalents of paraformaldehyde in MeCN was refluxed for 24 h, cooled to r.t. and poured into 5% HCl. The crude product was extracted with diethyl ether, dried over MgSO\textsubscript{4} and the solvent removed under vacuum. The yellow oil residue was purified by silica gel flash column chromatography.

General Method C.\textsuperscript{34} 1.1 equivalents of fuming HNO\textsubscript{3} was added dropwise to the corresponding hydroxybenzaldehyde in glacial acetic acid. After stirring at r.t. for 2 h, water was added to the reaction mixture and a white precipitate formed. The crude product was collected by filtration and recrystallized from hot EtOH by addition of cold water.

General Method D.\textsuperscript{34} 6 equivalents of sodium dithionite (Na\textsubscript{2}S\textsubscript{2}O\textsubscript{4}) was added to the corresponding 2-hydroxy-3-nitrobenzaldehyde in EtOH and water. The reaction mixture was refluxed for 2 h, cooled to r.t. and the solvent removed under vacuum.

General Method E.\textsuperscript{110} One equivalent of 5-bromo-2-hydroxy-3-nitrobenzaldehyde, C-3, 1.2 equivalents of the corresponding boronic acid, 6 equivalents of sodium carbonate and 0.05 equivalent of tetrakis(triphenylphosphine)palladium(0) were dissolved/suspended in DMF / water (1:1). The reaction mixture was heated at 105 °C under N\textsubscript{2} for 6 h. After cooling to r.t., 1 M NaOH was added to the reaction mixture which was then washed with DCM. The aqueous phase was acidified with 6 M HCl to give an orange/yellow precipitate which was washed with water and diethyl ether and then the solvent removed under vacuum.
5-\textit{(}tert\text{-}butyl\text{)}\textemdash 2\text{-}Hydroxybenzaldehyde, C-1

\begin{center}
\text{\textbf{General Method A.}}
\end{center}

4-\textit{tert\text{-}butylphenol} (2.00 g, 13.3 mmol) THF (70.0 mL). Eluent: DCM. The first fraction was the yellow oil product and the second fraction was the unreacted 4-\textit{tert\text{-}butylphenol}. Yield: 1.33 g, 56%

HRMS (ESI)

\begin{itemize}
  \item [M+H]\textsuperscript{+} 179.1062 (measured), 179.1067 m/z (calculated): C\textsubscript{11}H\textsubscript{15}O\textsubscript{2}
  \item [M+Na]\textsuperscript{+} 201.0879 m/z (measured), 201.0886 m/z (calculated): C\textsubscript{11}H\textsubscript{14}O\textsubscript{2}Na
  \item [M-H]\textsuperscript{-} 177.0921 m/z (measured), 177.0921 m/z (calculated): C\textsubscript{11}H\textsubscript{13}O\textsubscript{2}
\end{itemize}

GC-MS: 178.1 m/z (measured), 178.1 m/z (calculated): C\textsubscript{11}H\textsubscript{14}O\textsubscript{2}

\begin{itemize}
  \item \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ = 10.86 (s, 1 H, \textit{Ha}), 9.87 (s, 1 H, \textit{H1}), 7.59 (dd, 1 H, \textsuperscript{4}J = 2.5 Hz, \textit{H5}), 7.51, (d, 1 H, \textsuperscript{4}J = 2.5 Hz, \textit{H3}), 6.93 (d, 1 H, \textsuperscript{3}J = 8.8 Hz, \textit{H6}), 1.32 (s, 9 H, \textit{H9})
  \item \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ = 196.88 (\textit{C1}), 159.75 (\textit{C7}), 142.81 (\textit{C2}), 134.74 (\textit{C5}), 129.83 (\textit{C3}), 120.12 (\textit{C4}), 117.29 (\textit{C6}), 34.15 (\textit{C8}), 31.31 (\textit{C9})
\end{itemize}
5-(tert-butyl)-2-Hydroxy-3-nitrobenzaldehyde, **C-2**

![Chemical structure of 5-(tert-butyl)-2-Hydroxy-3-nitrobenzaldehyde]

**General Method C.**

5-(tert-butyl)-2-hydroxybenzaldehyde, **C-1** (1.00 g, 5.61 mmol), glacial acetic acid (10.0 mL) and water (20.0 mL). Yield: 0.653 g, 52%

**HRMS (ESI)**

[M+Na]$^+$ 246.0749 m/z (measured), 246.0737 m/z (calculated): C$_{11}$H$_{13}$NO$_4$Na

[M-H]$^-$ 222.0771 m/z (measured), 222.0772 m/z (calculated): C$_{11}$H$_{12}$NO$_4$

**GC-MS:** 223.0 m/z (measured), 223.0 m/z (calculated): C$_{11}$H$_{13}$NO$_4$

$^1$H NMR (300 MHz, CDCl$_3$): δ = 11.22 (s, 1 H, $H_a$), 10.41 (s, 1 H, $H_1$), 8.34 (d, 1 H, $^4J$ = 2.6 Hz, $H_5$), 8.14 (d, 1 H, $^4J$ = 2.6 Hz, $H_3$), 1.35 (s, 9 H, $H_9$)

$^{13}$C NMR (75 MHz, CDCl$_3$): δ = 189.49 (C1), 154.75 (C7), 143.69 (C2), 134.93 (C6), 134.46 (C5), 128.09 (C3), 125.22 (C4), 34.75 (C8), 31.12 (C9)
5-Bromo-2-hydroxy-3-nitrobenzaldehyde, C-3

![Chemical structure of 5-Bromo-2-hydroxy-3-nitrobenzaldehyde]

**General Method C.**
5-bromosalicylaldehyde (10.0 g, 49.8 mmol), acetic acid (50.0 mL) and cold water (250 mL). The crude product in an aqueous solution was extracted with ethyl acetate. Yellow solid product. The product was used for the next reaction without further purification. Yield: 12.0g, 98%.

HRMS (ESI)
[M-H]^- 245.9243 m/z (measured), 245.9231 m/z (calculated): C\textsubscript{7}H\textsubscript{5}BrNO\textsubscript{4}

\( ^1\text{H NMR} \) (300 MHz, CDCl\textsubscript{3}): \( \delta = 11.24 \) (s, 1 H, \( H_a \)), 10.36 (s, 1 H, \( H_I \)), 8.46 (d, 1 H, \( ^4J = 2.5 \) Hz, \( H_5 \)), 8.20 (d, 1 H, \( ^4J = 2.5 \) Hz, \( H_3 \))

\( ^{13}\text{C NMR} \) (75 MHz, CDCl\textsubscript{3}): \( \delta = 187.5 \) (\( C_1 \)), 155.47 (\( C_7 \)), 139.58 (\( C_3 \)), 134.63 (\( C_6 \)), 133.47 (\( C_5 \)), 126.95 (\( C_2 \)), 111.97 (\( C_4 \))
2-Hydroxy-5-methoxybenzaldehyde, C-4

General Method B.

4-methoxyphenol (3.00 g, 24.2 mmol), MeCN (100 mL) and 5% HCl (300 mL). Purified by flash silica column chromatography eluted with 20% EtOAc in n-hexane. The first fraction was the yellow oil product and the second fraction was the unreacted 4-methoxyphenol. Yield: 2.77 g, 75%

HRMS (ESI)  
[M-H] - 151.0406 m/z (measured), 151.0401 m/z (calculated): C₈H₇O₃
GC-MS: 152.0 m/z (measured), 152.0 m/z (calculated): C₈H₇O₃

¹H NMR (300 MHz, CDCl₃): δ = 10.64 (s, 1 H, H₄), 9.86 (s, 1 H, H₁), 7.17 (dd, 1 H, J = 3.0 Hz, H₅), 7.01 (d, 1 H, J = 3.0 Hz, H₃), 6.95 (d, 1 H, J = 9.0 Hz, H₆), 3.82 (s, 3 H, H₈)

¹³C NMR (75 MHz, CDCl₃): δ = 196.26 (C₁), 156.24 (C₇), 152.90 (C₄), 125.41 (C₅), 120.20 (C₂), 118.89 (C₃), 115.35 (C₆), 56.09 (C₈)
2-Hydroxy-5-methoxy-3-nitrobenzaldehyde, C-5

![Chemical Structure]

**General Method C.**

2-hydroxy-5-methoxybenzaldehyde, C-4 (1.00 g, 6.57 mmol), glacial acetic acid (10.0 mL) and water (20.0 mL). Yield: 0.451 g, 35%

**HRMS (ESI)**

[M+Na]^+ 220.0219 m/z (measured), 220.0216 m/z (calculated): C₈H₇NO₅Na

[M-H]^- 196.0260 m/z (measured), 196.0251 m/z (calculated): C₈H₆NO₅

**GC-MS**: 197.0 m/z (measured), 197.0 m/z (calculated): C₈H₇NO₅

**¹H NMR (300 MHz, CDCl₃)**: δ = 10.88 (s, 1 H, Ha), 10.44 (s, 1 H, H1), 7.85 (d, 1 H, 4J = 3.2 Hz, H5), 7.72 (d, 1 H, 4J = 3.2 Hz, H3), 3.87 (s, 3 H, H9)

**¹³C NMR (75 MHz, CDCl₃)**: δ = 188.25 (C1), 152.20 (C7), 151.27 (C4), 134.62 (C6), 126.34 (C2), 123.06 (C3), 115.36 (C5), 56.52 (C8)
Potassium 4-hydroxyphenyl sulfate, C-6^11^1

K$_2$S$_2$O$_8$ (2.70 g, 10 mmol) in water (50.0 mL) was added dropwise over a period of 2 h to phenol (0.940, 10 mmol) and NaOH (2.00 g, 50 mmol) in water (20.0 mL) with vigorous stirring. A water bath was used to maintain the temp at 20 °C. The solution slowly changed from colourless to dark brown in colour. After the addition was completed, the reaction mixture was stirred at r.t. for 24 h and neutralised by adding dilute HCl until the pH reached 7. Unreacted phenol was removed by extraction with diethyl ether and the combined aqueous phases were evaporated under vacuum and extracted with EtOH using an ultra-sonic bath to a give light brown solid. This crude product was used for further reaction without purification. Yield: 0.865 g, 38%

HRMS (ESI)
[M]$^-1$ 188.9868 m/z (measured), 188.9863 m/z (calculated): C$_6$H$_5$O$_5$S

$^1$H NMR (300 MHz, DMSO): δ = 6.91 (d, 2 H, $^3$J = 8.8 Hz, $H1$), 6.60 (d, 2 H, $^3$J = 8.8 Hz, $H2$)

$^{13}$C NMR (75 MHz, DMSO): δ = 153.30 (C4), 145.69 (C3), 121.99 (C2), 114.93 (C1)
Ethyl 2-(4-(benzoyloxy)phenoxy)acetate, C-7

4-(benzoyloxy)Phenol (0.200 g, 1 mmol), ethyl 2-bromoacetate (0.110 mL, 1 mmol) and K₂CO₃ (0.276 g, 2 mmol) in acetone (15.0 mL) was refluxed for 3 h. After cooling to r.t., the reaction mixture was quenched with water (10.0 mL) and acidified with 1 M HCl to pH 3. Acetone was then removed under reduced pressure. The aqueous solution was extracted with diethyl ether, dried over Na₂SO₄ and evaporated under vacuum. The crude product was purified by flash column chromatography (eluent: 20% EtOAc in n-hexane) and the 2nd fraction was the product isolated as a colourless oil. Yield: 0.232 g, 81%

HRMS (ESI)
[M+H]^+ 287.1273 m/z (measured), 287.1278 m/z (calculated): C₁₇H₁₉O₄
[M+Na]^+ 309.1092 m/z (measured), 309.1097 m/z (calculated): C₁₇H₁₈O₄Na

¹H NMR (500 MHz, CDCl₃): δ =7.44 (m, 5 H, H7,8,9), 6.93 (m, 4 H, H1,2), 5.00 (s, 2 H, H5), 4.57 (s, 2 H, Ha), 4.29 (q, 2 H, ²J = 6.8 Hz, He), 1.31 (t, 3 H, ³J = 6.8 Hz, Hd)

¹³C NMR (125 MHz, CDCl₃): δ =169.23 (Cb), 153.81 (C3), 152.33 (C4), 137.23 (C6), 128.61 (C7,8,9), 127.97 (C7,8,9), 127.52 (C7,8,9), 115.94 (C1,2), 115.89 (C1,2), 70.66 (Ca), 66.38 (C5), 61.32 (Cc), 14.21 (Cd)
Ethyl 2-((4-(benzyloxy)phenoxy)propanoate, C-8\textsuperscript{112}

4-(benzyloxy)Phenol (2.00 g, 10 mmol), ethyl 2-bromopropanoate (1.30 mL, 10 mmol) and K\textsubscript{2}CO\textsubscript{3} (2.76 g, 20 mmol) in acetone (150 mL) was refluxed for 5 h. After cooled to r.t., the reaction mixture was quenched with water (100 mL) and acidified with 1 M HCl to pH 3. Acetone was then removed under reduced pressure. The aqueous solution was extracted with diethyl ether, dried over Na\textsubscript{2}SO\textsubscript{4} and evaporated under vacuum. The crude product was purified by flash column chromatography (eluent: 20\% EtOAc in n-hexane) and the 2\textsuperscript{nd} fraction was the product. Yield: 2.62 g, 87\%

HRMS (ESI) [M+Na]\textsuperscript{+} 323.1254 m/z (measured), 323.1254 m/z (calculated): C\textsubscript{18}H\textsubscript{20}O\textsubscript{4}Na

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): δ = 7.42 (m, 5 H, H\textsubscript{7,8,9}), 6.89 (m, 4 H, H\textsubscript{1,2}), 5.00 (s, 2 H, H\textsubscript{5}), 4.67 (q, 1 H, \textsuperscript{3}J = 6.7 Hz, H\textsubscript{a}), 4.38 (q, 2 H, \textsuperscript{3}J = 6.8 Hz, H\textsubscript{c}), 1.59 (d, 3 H, \textsuperscript{3}J = 6.7 Hz, H\textsubscript{b}), 1.26 (t, 3 H, \textsuperscript{3}J = 6.8 Hz, H\textsubscript{d})

\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): δ = 172.46 (Ce), 153.73 (C3), 152.01 (C4), 137.27 (C6), 128.61 (C7,8,9), 127.96 (C7,8,9), 127.53 (C7,8,9), 116.55 (C1,2), 115.86 (C1,2), 73.66 (Ca), 70.65 (C5), 61.24 (Ce), 18.67 (Cb), 14.21 (Cd)
Ethyl 2-(4-hydroxyphenoxy)acetate, C-9

![Chemical Structure](image)

Method 1.¹¹¹
Potassium 4-hydroxyphenyl sulfate, C-6 (2.00 g, 8.76 mmol), ethyl 2-bromoacetate (0.970 mL, 8.76 mmol) and K₂CO₃ (2.36 g, 8.76 mmol) in EtOH (80 mL) was refluxed for 6 h. The solvent was removed under vacuum. The residue was redissolved in acetic acid (80 mL) and the reaction mixture was refluxed for 2 h. The solvent was removed under vacuum and the residue was redissolved in water (100 mL). The product was extracted with DCM (2 x 150 mL) and the extract was washed with water multiple times, dried over MgSO₄ and the solvent removed under vacuum to give a yellow oil which was used for further reaction without purification (it can be purified by flash column chromatography).
Yield: 0.330 g, 19%

Method 2.
Ethyl 2-(4-hydroxyphenoxy)acetate, C-10 (0.232 g, 1.18 mmol) and Pd/C (0.023 g, 10% in mass) were dissolved/suspended in EtOH (50.0 mL). The reaction mixture was stirred at r.t. overnight under a H₂ atmosphere using a balloon. After filtration through Celite, the filtrate was evaporated under vacuum to give a colourless oil. Yield: 0.229 g, 99%

HRMS (ESI)
[M+Na]⁺ 219.0624 m/z (measured), 219.0628 m/z (calculated): C₁₀H₁₂O₄Na

¹H NMR (500 MHz, CDCl₃): δ = 6.81 (dd, 4 H, J = 9.0 Hz, H₁,2), 4.55 (s, 2 H, Ha), 4.28 (q, 2 H, J = 7.3 Hz, Hc), 1.30 (t, 3 H, J = 7.3 Hz, Hd)

¹³C NMR (125 MHz, CDCl₃): δ = 169.58 (Ca), 152.08 (C₄), 150.43 (C₃), 116.25 (C₂), 116.19 (C₁), 66.54 (Ca), 61.52 (Cc), 14.27 (Cd)
** tert-Butyl 2-(4-hydroxyphenoxy)acetate, C-10**

\[
\begin{array}{c}
\text{OH} \\
\text{3} \\
\text{2} \\
\text{4} \\
\text{1} \\
\text{a} \\
\text{b} \\
\text{c} \\
\text{d}
\end{array}
\]

Hydroquinone (0.220 g, 2 mmol) and sodium hydroxide (0.170 g, 4 mmol) in a mixture of dioxane (4 mL) / water (4.00 mL) were degassed under N\(_2\) atmosphere for 30 min. tert-butyl bromoacetate (0.300 mL, 2 mmol) was added to the reaction mixture which was then stirred at r.t. for 3 h, acidified with 3 M HCl up to pH 3, extracted with diethyl ether, dried over Na\(_2\)SO\(_4\) and evaporated under vacuum. The residue was purified by flash silica column chromatography (eluent: 20% EtOAc in n-hexane) to give a brown solid. Yield: 280 mg, 63%

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 6.80 \text{ (s, 2 H, } H2), 6.73 \text{ (s, 2 H, } H1), 4.44 \text{ (s, 2 H, } Ha), 1.46 \text{ (s, 9 H, } Hd)\)

\(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 168.95 \text{ (Cb), 152.76 (C3), 151.84 (C4), 116.19 (C2), 115.79 (C1), 82.64 (Cc), 66.71 (Ca), 28.10 (Cd)\)
Ethyl 2-(4-hydroxyphenoxy)propanoate, **C-11**

![Diagram of C-11](image)

**Method 1.**

Potassium 4-hydroxyphenyl sulfate, **C-6** (8.00 g, 35.1 mmol), ethyl 2-bromopropanoate (4.55 mL, 35.1 mmol) and \( \text{K}_2\text{CO}_3 \) (9.47, 35.1 mmol) in EtOH (100 mL) was refluxed for 6 h. The solvent was removed under vacuum. The residue was redissolved in acetic acid (100 mL) and the reaction mixture was refluxed for 2 h. The solvent was removed under vacuum and the residue was redissolved in water (200 mL). The product was extracted with DCM (200 mL x 3) and the extract was washed with water multiple times, dried over MgSO\(_4\) and dried under vacuum to give yellow oil which was used for the further reaction without purification. Yield: 1.02 g, 14%

**Method 2.**

Ethyl 2-(4-(benzyloxy)phenoxy)propanoate, **C-7** (2.62 g, 8.72 mmol) and Pd/C (0.262 g 10% in mass) were dissolved/suspended in EtOH (150 mL). The reaction mixture was stirred at r.t. overnight under H\(_2\) atmosphere at a balloon pressure. After filtration through Celite, the filtrate was evaporated under vacuum to give a colourless oil. Yield: 1.81 g, 99%.

**HRMS (ESI)**

\[ \text{[M+Na]}^+ 233.0783 \text{ m/z (measured)}, 233.0784 \text{ m/z (calculated): C}_11\text{H}_{14}\text{O}_4\text{Na} \]

\[ \text{[M+K]}^+ 249.0533 \text{ m/z (measured)}, 249.0524 \text{ m/z (calculated): C}_11\text{H}_{14}\text{O}_4\text{K} \]

**GC-MS:** 210.1 m/z (measured), 210.1 m/z (calculated): C\(_{11}\)H\(_{14}\)O\(_4\)

\(^1\text{H NMR (400 MHz, CDCl}_3\): } \delta = 6.78 \text{ (dd, 4 H, } ^3\text{J} = 9.1 \text{ Hz, } \text{H}_1,\text{H}_2), 4.66 \text{ (q, 1 H, } ^3\text{J} = 6.7 \text{ Hz, } \text{H}_a), 4.25 \text{ (q, 2 H, } ^3\text{J} = 7.3 \text{ Hz, } \text{H}_c), 1.59 \text{ (d, 3 H, } ^3\text{J} = 6.7 \text{ Hz, } \text{H}_b), 1.26 \text{ (t, 3 H, } ^3\text{J} = 7.3 \text{ Hz, } \text{H}_d) \]

\(^{13}\text{C NMR (100 MHz, CDCl}_3\): } \delta = 151.86 \text{ (C}_3\), 150.43 \text{ (C}_4\), 116.87 \text{ (C}_2\), 116.21 \text{ (C}_1\), 73.86 \text{ (C}_a\), 61.40 \text{ (C}_c\), 18.73 \text{ (C}_d\), 14.26 \text{ (C}_b\)
Ethyl 2-(3-formyl-4-hydroxyphenoxy)acetate, C-12 (NEW)

General Method A.\textsuperscript{109}

Ethyl 2-(4-hydroxyphenoxy)acetate, C-9 (1.80 g, 9.17 mmol), THF (80.0 mL) and 5% HCl (150 mL). Purified by flash silica column chromatography (eluent= 10% EtOAc in DCM) to give a yellow oil product. The first fraction was the product. Yield: 0.380 g, 18.5%

HRMS (ESI) 
[M+Na]\textsuperscript+ 247.0573 m/z (measured), 247.0577 m/z (calculated): C\textsubscript{11}H\textsubscript{12}O\textsubscript{5}Na

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ = 10.62 (s, 1 H, Ha), 9.77 (s, 1 H, H1), 7.16 (dd, 1 H, \textsuperscript{4}J = 3.0 Hz, H5), 7.00 (d, 1 H, \textsuperscript{3}J = 3.0 Hz, H3), 6.89 (d, 1 H, \textsuperscript{3}J = 9.0 Hz, H6), 4.56 (s, 2 H, H8), 4.25 (q, 2 H, \textsuperscript{3}J = 7.1 Hz, H10), 1.27 (t, 3 H, \textsuperscript{3}J = 7.1 Hz, H11)

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ = 195.99 (C1), 168.70 (C9), 156.70 (C7), 151.00 (C4), 125.87 (C5), 120.06 (C2), 118.83 (C3), 117.22 (C6), 66.37 (C8), 61.44 (C10), 14.13 (C11)
tert-Butyl 2-(3-formyl-4-hydroxyphenoxy)acetate, C-13 (NEW)

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
6 & \quad 7 & \quad 1 \\
5 & \quad 4 & \quad 3 \\
& \quad \text{O} & \quad \text{O} \\
8 & \quad 9 & \quad 10 & \quad 11
\end{align*}
\]

**General Method C.**

tert-Butyl 2-(4-hydroxyphenoxy)acetate, C-10 (0.280 g, 1.25 mmol), THF (30.0 mL) and 3 N HCl (2.00 mL). Purified by flash silica column chromatography (eluent= 10% EtOAc in DCM) to give a yellow oil product. The first fraction was the product. Yield: 0.073 g, 23%

HRMS (ESI)  
\[\text{[M+Na]}^+ \ 275.0885 \text{ m/z (measured)}, 275.0890 \text{ m/z (calculated): } C_{13}H_{16}O_5Na\]

\(^1\text{H NMR (500 MHz, CDCl}_3\): } \delta = 10.60 (s, 1 H, \text{H}a), 9.76 (s, 1 H, \text{H}I), 7.13 (dd, 1 H, \text{J} J = 3.1 \text{ Hz, H}5), 6.97 (d, 1 H, \text{J} J = 3.1 \text{ Hz, H}3), 6.88 (d, 1 H, \text{J} J = 9.0 \text{ Hz, H}6), 4.46 (s, 2 H, H8), 1.43 (s, 9 H, H11)

\(^{13}\text{C NMR (125 MHz, CDCl}_3\): } \delta = 195.99 (\text{C}1), 167.79 (\text{C}9), 156.55 (\text{C}7), 151.07 (\text{C}4), 125.74 (\text{C}5), 120.03 (\text{C}2), 118.76 (\text{C}3), 117.20 (\text{C}6), 82.52 (\text{C}10), 66.60 (\text{C}8), 28.01 (\text{C}11)\]
Ethyl 2-(3-formyl-4-hydroxyphenoxy)propanoate, C-14 (NEW)

\[
\begin{align*}
\text{OH} & \quad \text{O} \\
6 & \quad 7 \\
\text{O} & \quad \text{O} \\
8 & \quad 9 \\
\text{O} & \quad \text{O} \\
10 & \quad 11 \\
2 & \quad 1 \\
3 & \quad 4 \\
5 & \quad 6 \\
8 & \quad 9 \\
10 & \quad 11 \\
2 & \quad 1 \\
3 & \quad 4 \\
5 & \quad 6
\end{align*}
\]

**General Method B.**

Ethyl 2-(4-hydroxyphenoxy)propanoate, C-11 (2.52 g, 12 mmol), MeCN (100 mL), and 5% HCl (150 mL). Eluent: 10% EtOAc in \(n\)-hexane. The first fraction was the yellow oil product. Yield: 0.670 g, 24%

**HRMS (ESI)**

\([\text{M+Na}]^+ 261.0737 \text{ m/z (measured)}, \text{261.0744 m/z (calculated): C}_{12}\text{H}_{14}\text{O}_5\text{Na}

**GC-MS:** 238.1 m/z (measured), 238.1 m/z (calculated): C_{12}H_{14}O_5

\(^1\text{H NMR (400 MHz, CDCl}_3\):} \delta = 10.53 (s, 1 H, \text{Ha}), 9.69 (s, 1 H, \text{H1}), 7.06 (dd, 1 H, \text{^4J = 3.0 Hz, H5}), 6.92 (d, 1 H, \text{^4J = 3.0 Hz, H3}), 6.79 (d, 1 H, \text{^3J = 8.9 Hz, H6}), 4.62 (q, 1 H, \text{^3J = 6.7 Hz, H8}), 4.13 (q, 2 H, \text{^3J = 7.0 Hz, H11}), 1.51 (d, 3 H, \text{^3J = 6.7 Hz, H9}), 1.15 (t, 3 H, \text{^3J = 7.0 Hz, H12})

\(^{13}\text{C NMR (100 MHz, CDCl}_3\):} \delta = 195.916 (\text{C1}), 171.64 (\text{C10}), 156.43 (\text{C7}), 150.51 (\text{C4}), 126.23 (\text{C5}), 119.96 (\text{C2}), 118.54 (\text{C3}), 117.88 (\text{C6}), 73.66 (\text{C8}), 61.16 (\text{C11}), 18.29 (\text{C9}), 13.94 (\text{C12})
Ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxo)acetate, C-15 (NEW)

![Chemical structure]

**General Method C.**
Ethyl 2-(3-formyl-4-hydroxyphenoxy)acetate, C-12 and acetic acid (2.00 mL) and water (100 mL), Purified by recrystallization from chloroform to give a yellow solid. Yield: 0.184 g, 40%

**HRMS (ESI)**
[M+Na]$^+$ 292.0439 m/z (measured), 292.0428 m/z (calculated): C$_{11}$H$_{11}$NO$_7$Na

$^1$H NMR (300 MHz, CDCl$_3$): δ = 10.91 (s, 1 H, Ha), 10.42 (s, 1 H, H1), 7.90 (d, 1 H, $^4$J = 3.1 Hz, H5), 7.72 (d, 1 H, $^4$J = 3.2 Hz, H3), 4.67 (s, 2 H, H8), 4.31 (q, 2 H, $^3$J = 7.1 Hz, H10), 1.33 (t, 3 H, $^3$J = 7.1 Hz, H11)

$^{13}$C NMR (75 MHz, CDCl$_3$): δ = 187.97 (C1), 167.92 (C9), 151.85 (C7), 150.39 (C4), 134.75 (C6) (found in HMBC), 126.38 (C2), 123.56 (C3), 116.97 (C5), 66.22 (C8), 61.97 (C10), 14.28 (C11)
**General Method C.**

tert-Butyl 2-(3-formyl-4-hydroxyphenoxy)acetate, C-13 (0.073 g, 0.089 mmol), acetic acid (1.00 mL) and water (20.0 mL). Purified by flash silica column chromatography (eluent: 33% EtOAc in DCM) to give a yellow/orange oil. The 2\textsuperscript{nd} fraction was the product. Yield: 0.027 g, 64% 

HRMS (ESI)  
\[ \text{[M+Na]}^+ \text{ 320.0736 m/z (measured), 320.0741 m/z (calculated): C}_{13}\text{H}_{15}\text{NO}_7\text{Na} \]

\( ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 10.90 \text{ (s, 1 H, } H_a) , 10.43 \text{ (s, 1 H, } H_1) , 7.88 \text{ (d, 1 H, } ^4J = 3.2 \text{ Hz, } H_5) , 7.71 \text{ (d, 1 H, } ^4J = 3.2 \text{ Hz, } H_3) , 4.57 \text{ (s, 2 H, } H_8) , 1.50 \text{ (s, 9 H, } H_{11}) \)
Ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy)propanoate, C-17 (NEW)

\[
\begin{array}{c}
\text{O}_2\text{N} \\
\text{H} \\
\text{OH} \\
\text{3} \\
\text{2} \\
\text{1} \\
\text{O} \\
\text{4} \\
\text{5} \\
\text{6} \\
\text{7} \\
\text{8} \\
\text{9} \\
\text{10} \\
\text{11} \\
\text{12} \\
\end{array}
\]

Method 1.
Ethyl 2-(3-formyl-4-hydroxyphenoxy)propanoate, C-14 (0.100 g, 0.42 mmol) was dissolved in conc. H\text{2}SO\text{4} (1.00 mL). 69% HNO\text{3} (0.100 mL, 1.20 mmol) was added dropwise to the mixture at 0 °C. After 2 h stirring at r.t., the reaction mixture was quenched with cold water (200 mL) to give orange precipitate which was extracted with DCM, dried over Na\text{2}SO\text{4} and the solvent removed under vacuum. The crude product was purified by Silica gel flash column chromatography eluted with DCM. The second fraction was the yellow oil product. Yield: 26.0 mg, 22%

Method 2. **General Method C.**
Ethyl 2-(3-formyl-4-hydroxyphenoxy)propanoate, C-14 (0.467 g, 1.96 mmol), acetic acid (2.00 mL) and water (100 mL). An orange oil product. Yield: 0.251 g, 45%

**HRMS (ESI)**
\[ [\text{M+Na}]^+ 306.0573 \text{ m/z (measured), 306.0584 m/z (calculated): C}_{12}\text{H}_{13}\text{NO}_7\text{Na} \]

\(^1\text{H NMR (300 MHz, CDCl}_3\text{):} \delta = 10.90 (s, 1 \text{ H, } \text{H}_a), 10.41 (s, 1 \text{ H, } \text{H}_1), 7.87 (d, 1 \text{ H, } ^4\text{J} = 3.1 \text{ Hz, } \text{H}_5), 7.69 (d, 1 \text{ H, } ^4\text{J} = 3.1 \text{ Hz, } \text{H}_3), 4.79 (q, 1 \text{ H, } ^3\text{J} = 6.8 \text{ Hz, } \text{H}_8), 4.27 (q, 2 \text{ H, } ^3\text{J} = 7.1 \text{ Hz, } \text{H}_{11}), 1.66 (d, 3 \text{ H, } ^3\text{J} = 6.8 \text{ Hz, } \text{H}_9), 1.30 (t, 3 \text{ H, } ^3\text{J} = 7.1 \text{ Hz, } \text{H}_{12}) \]

\(^{13}\text{C NMR (75 MHz, CDCl}_3\text{):} \delta = 188.04 (\text{C}_1), 171.02 (\text{C}_{10}), 151.75 (\text{C}_7), 150.17 (\text{C}_4), 135.31 (\text{C}_6) \text{ (found in HMBC), 126.32 (C}_2\text{), 124.22 (C}_3\text{), 117.44 (C}_5\text{), 73.93 (C}_8\text{), 61.93 (C}_{11}\text{), 29.84 (C}_{12}\text{), 18.44 (C}_9\text{)} \]
2-(3-formyl-4-hydroxy-5-nitrophenoxy)Acetic acid, **C-18 (NEW)**

![Chemical Structure]

**Method 1.**

1 M NaOH (40.0 mL) was added to a solution of ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy)acetate, **C-15** (0.184 g, 0.683 mmol) in MeOH (50.0 mL). The yellow/orange solution turned to dark red in colour immediately after the addition of 1 M NaOH. The reaction mixture was stirred at r.t. overnight. MeOH was removed under reduced pressure. 1 M HCl (25.0 mL) was added to the remaining solution to form a yellow solution (pH 1) which was extracted with DCM, dried over Na₂SO₄ and the solvent removed under vacuum to give yellow oily solid. Yield: 0.164 g, 100%. If needed, the product can be purified further by flash silica column chromatography using DCM as an eluent.

**Method 2.**

**tert-Butyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy)acetate, C-16** (0.027 g, 0.091 mmol) was dissolved in DCM (5.00 mL) and TFA (0.020 mL, 0.272 mmol) was added at r.t. The reaction mixture was then stirred at r.t. overnight. The solvent was removed under vacuum and the remaining acid was co-evaporated with dioxane twice to give a yellow oil. Yield: 0.021 g, 96%.

**HRMS (ESI)**

[M-H]⁻ 240.0168 m/z (measured), 240.0150 m/z (calculated): C₉H₆NO₇

**¹H NMR (500 MHz, CDCl₃):** δ = 11.85 (s, 1 H, Hb), 10.95 (s, 1 H, Ha), 10.45 (s, 1 H, H1), 7.94 (d, 1 H, J = 3.4 Hz, H5), 7.77 (d, 1 H, J = 3.4 Hz, H3), 4.76 (s, 2 H, H8)

**¹³C NMR (125 MHz, CDCl₃):** δ = 187.96 (C1), 172.38 (C9), 151.94 (C7), 150.19 (C4), 126.43 (C2), 124.29 (C6), 123.48 (C3), 117.70 (C5), 65.67 (C8)
2-(3-formyl-4-hydroxy-5-nitrophenoxy)propanoic acid, C-19 (NEW)

![Chemical structure](image)

1 M NaOH (80.0 mL) was added to a solution of ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxy)propanoate, C-17 (0.356 g, 1.26 mmol) in MeOH (100 mL). The yellow/orange solution turned to dark red in colour immediately after the addition of 1 M NaOH. The reaction mixture was stirred at r.t. overnight. MeOH was removed under reduced pressure. 1 M HCl (50.0 mL) was added to the remaining solution to form a yellow solution (pH 1) which was extracted with DCM, dried over Na₂SO₄ and the solvent removed under vacuum to give yellow oily solid. Yield: 0.320 g, 100%.

HRMS (ESI)

[M+Na]⁺ 278.0273 m/z (measured), 278.0271 m/z (calculated): C₁₀H₈NO₇

¹H NMR (500 MHz, CDCl₃): δ = 10.91 (s, 1 H, Ha), 10.41 (s, 1 H, H1), 7.89 (d, 1 H, J = 3.0 Hz, H5), 7.70 (d, 1 H, J = 3.0 Hz, H3), 4.85 (q, 1 H, J = 7.0 Hz, H8), 1.70 (d, 3 H, J = 7.0 Hz, H9)

¹³C NMR (125 MHz, CDCl₃): δ = 188.12 (C1), 175.72 (C10), 151.94 (C7), 149.87 (C4), 135.06 (C6), 126.36 (C2), 124.05 (C3), 117.70 (C5), 73.33 (C8), 18.37 (C9)
3'-Formyl-4'-hydroxy-5'-nitro-[1,1'-biphenyl]-4-carboxylic acid, C-20

![Chemical structure](image)

**General Method E.**

4-carboxyphenylboronic acid (0.199 g, 1.2 mmol), DMF (20.0 mL) / water (20.0 mL), 1 M NaOH (20.0 mL), DCM (10.0 mL x 3), 6 M HCl (20.0 mL) and diethyl ether (5.00 mL x 3). Yield: 0.176 g, 61%

HRMS (ESI)

[M-H]⁻ 286.0355 m/z (measured), 286.0357 m/z (calculated): C₁₄H₈NO₆

¹H NMR (300 MHz, DMSO): δ = 13.04 (s, 1 H, Hb), 10.33 (s, 1 H, H1), 8.58 (d, 1 H, ²J = 2.5 Hz, H5), 8.39 (d, 1 H, ²J = 2.5 Hz, H3), 8.06 (dd, 2 H, ²J = 1.8 Hz, H10), 7.90 (dd, 2 H, ²J = 1.8 Hz, H9)
3'-Formyl-4'-hydroxy-5'-nitro-[1,1'-biphenyl]-4-carbonitrile, C-21 (NEW)

![Chemical Structure](image)

**General Method E.**

4-cyanophenylboronic acid (0.176 g, 1.2 mmol), DMF (20.0 mL) / water (20.0 mL), 1 M NaOH (20.0 mL), DCM (10.0 mL x 3), 6 M HCl (20.0 mL) and diethyl ether (5.00 mL x 3). Yield: 0.108 g, 40%

HRMS (ESI)

[M-H] - 267.0414 m/z (measured), 267.0411 m/z (calculated): C_{14}H_{7}N_{2}O_{4}

$^1$H NMR (300 MHz, DMSO): $\delta = 10.25$ (s, 1 H, H1), 8.25 (d, 1 H, $^4J = 2.9$ Hz, H5), 7.90 (d, 1 H, $^4J = 2.9$ Hz, H3), 7.76 (d, 4 H, $^3J = 2.0$ Hz, H9,10)

$^{13}$C NMR (125 MHz, DMSO): $\delta = 190.65$ (C1), 168.46 (C7), 143.78 (C8), 142.87 (C6), 132.71 (C10), 131.77 (C3), 130.43 (C5), 130.11 (C2), 125.27 (C9), 119.19 (C4), 114.63 (C12), 107.49 (C11)
2-Hydroxy-3-nitro-5-(pyridin-4-yl)benzaldehyde, C-22 (NEW)

General Method E.
4-pyridinylboronic acid (0.148 g, 1.2 mmol), DMF (20.0 mL) / water (20.0 mL), 6 M HCl (40.0 mL), DCM (10.0 mL x 3), 1 M NaOH (60.0 mL) and diethyl ether (5.00 mL x 3). Yield: 0.134 g, 56%

HRMS (ESI)
[M+H]$^+$ 245.0559 m/z (measured), 245.0557 m/z (calculated): C$_{12}$H$_9$N$_2$O$_4$
[M+Na]$^+$ 267.0377 m/z (measured), 267.0376 m/z (calculated): C$_{12}$H$_8$N$_2$O$_4$Na

$^1$H NMR (500 MHz, DMSO): $\delta$ = 10.25 (s, 1 H, H1), 8.47 (d, 2 H, $^3$J = 4.8 Hz, H10), 8.30 (d, 1 H, $^4$J = 4.8 Hz, H5), 7.95 (d, 1 H, $^4$J = 2.6 Hz, H3), 7.55 (d, 4 H, $^3$J = 2.6 Hz, H9)

$^{13}$C NMR (125 MHz, DMSO): $\delta$ = 190.56 (C1), 168.71 (C7), 149.97 (C10), 146.00 (C4), 143.11 (C6), 130.98 (C3), 130.05 (C5), 130.00 (C2), 118.96 (C9), 112.98 (C8)
3-Butyl-3'-formyl-4'-hydroxy-5'-nitro-[1,1'-biphenyl]-4-carboxylic acid, C-23

General Method E.
4-borono-2-butylbenzoic acid, B-4 (0.109 g, 0.491 mmol), DMF (10.0 mL) / water (10.0 mL), 1 M NaOH (10.0 mL), DCM (5.00 mL x 3), 6 M HCl (10.0 mL) and washing with water only. Yield: 0.167 g, 99%.

HRMS (ESI)
[M-H]⁻: 342.0994 m/z (measured), 342.0983 m/z (calculated): C₁₈H₁₆NO₆

¹H NMR (300 MHz, DMSO): δ = 12.87 (s, 1 H, Ha or b), 10.33 (s, 1 H, H1), 8.54 (d, 1 H, ²J = 2.5 Hz, H5), 8.34 (d, 1 H, ²J = 2.5 Hz, H3), 7.88 (d, 1 H, ³J = 8.1 Hz, H10), 7.68 (d, 1 H, ²J = 8.5 Hz, H13), 7.65 (dd, 1 H, ²J = 2.1 Hz, H9), 3.03 (t, 2 H, ²J = 8.0 Hz, H15), 1.60 (p, 2 H, ³J = 7.5 Hz, H16), 1.38 (s, 2 H, ³J = 7.5 Hz, H17), 0.93 (t, 3 H, ³J = 7.2 Hz, H18)
3'-Formyl-3-heptyl-4'-hydroxy-5'-nitro-[1,1'-biphenyl]-4-carboxylic acid, C-24 (NEW)

![Chemical Structure](image)

**General Method E.**

4-borono-2-heptylbenzoic acid, B-5 (0.100 g, 0.379 mmol), DMF (8.00 mL) / water (8.00 mL), 1 M NaOH (8.00 mL), DCM (3 x 4.00 mL), 6 M HCl (8.00 mL) and washing with water only. Yield: 0.113 g, 93%

HRMS (ESI)

[M+Na]^+ 408.1404 m/z (measured), 408.1418 m/z (calculated): C_{21}H_{23}NO_{6}Na

^1H NMR (300 MHz, CDCl₃): δ = 11.41 (s, 1 H, Hₐ or b), 10.50 (s, 1 H, H₁), 8.61 (d, 1 H, ^3J = 2.5 Hz, H₅), 8.39 (d, 1 H, ^3J = 2.5 Hz, H₃), 8.16 (d, 1 H, ^3J = 8.8 Hz, H₁₀), 7.52 (d, 1 H, ^3J = 1.9 Hz, H₉), 7.49 (s, 1 H, H₁₃), 3.13 (t, 2 H, ^3J = 7.6 Hz, H₁₅), 1.72 (p, 2 H, ^3J = 6.7 Hz, H₁₆), 1.45 – 1.30 (m, 8 H, H₁₇, 1₈, 1₉, 2₀), 0.91 (t, 3 H, ^3J = 6.6 Hz, H₂₁)

^13C NMR (75 MHz, CDCl₃): δ = 188.99 (C₁), 170.92 (C₁₄), 156.27 (C₇), 147.49 (C₁₂), 141.11 (C₈), 135.37 (C₃), 132.89 (C₁₀), 135.66 (C₆), 132.45 (C₄), 129.52 (C₁₃), 129.33 (C₅), 128.08 (C₁₁), 126.09 (C₂), 124.13 (C₉), 34.98 (C₁₅), 32.11 (C₁₆), 31.98 (C₁₇), 29.92 (C₁₈), 29.26 (C₁₉), 22.81 (C₂₀), 14.25 (C₂₁)
Penta(t-butyl)camperstarene, **Cam-1**

![Cam-1 molecule](image)

**General Method D.**

5-((tert-butyl)-2-hydroxy-3-nitrobenzaldehyde, **C-2** (0.200 g, 0.896 mmol), EtOH (20.0 mL) and water (3.00 mL). The purple crude product was purified by flash neutral alumina column chromatography (eluent: DCM/MeOH, 10/1). Yield: 0.154 g, 98%.

**HRMS (ESI)**

- [M+Na]$^+$ 898.4853 m/z (measured), 898.4878 m/z (calculated): C$_{55}$H$_{65}$N$_5$O$_5$Na
- [M+K]$^+$ 914.4599 m/z (measured), 914.4617 m/z (calculated): C$_{55}$H$_{65}$N$_5$O$_5$K
- [3M+2K]$^{2+}$ 1352.7239 m/z (measured), 1352.7126 m/z (calculated): C$_{165}$H$_{195}$N$_{15}$O$_{15}$K$_2$
- [5M+3K]$^{3+}$ 1499.1565 m/z (measured), 1499.1307 m/z (calculated): C$_{275}$H$_{325}$N$_{25}$O$_{25}$K$_3$

**IR:** $\nu = 2952, 2860, 1615, 1520, 1477, 1462, 1390, 1362, 1342, 1297, 1250, 1221, 1135, 1102, 1039, 1011, 940, 859, 832, 804, 784, 632, 603, 543, 510, 453$ cm$^{-1}$.

$^1$H NMR (300 MHz, DMSO): $\delta = 17.10$ (monomer, d, 5 H, $^3J = 5.4$ Hz, **OH**), 17.06 (dimer, d, 5 H, $^3J = 10.7$ Hz, **OH**), 9.45 (monomer, d, 5 H, $^3J = 5.8$ Hz, **HC=N**), 8.44 (dimer, d, 5 H, $^3J = 10.9$ Hz, **HC=N**), 8.02 (monomer, d, 5 H, $^3J = 2.1$ Hz, **Ar-H**), 7.58 (dimer, d, 5 H, $^3J = 2.1$ Hz, **Ar-H**), 7.51 (monomer, d, 5 H, $^3J = 2.0$ Hz, **Ar-H**), 7.01 (dimer, d, 5 H, $^3J = 2.0$ Hz, **Ar-H**), 1.49 (dimer, s, 45 H, **CH$_3$**), 1.39 (monomer, s, 45 H, **CH$_3$**)

Due to the very low solubility in organic solvents even in DMSO, $^{13}$C NMR spectrum does not show the quaternary carbons as addressed in the literature.$^{34}$
Pentamethoxy-campestarene, **Cam-3** (NEW)

![Chemical structure of Cam-3](image)

**General Method D.**

2-hydroxy-5-methoxy-3-nitrobenzaldehyde, **C-5** (0.182 g, 0.923 mmol) in EtOH (20.0 mL) and water (3.00 mL). The purple crude product was purified twice by Soxhlet technique using DCM and MeOH as solvents for 24 h each and multiple washing with water using an ultra-sonic bath. Yield: 0.082 g, 59%

MALDI-TOF-MS

- [M+H]^+ 746.3896 m/z (measured), 746.2462 m/z (calculated): C\textsubscript{40}H\textsubscript{36}N\textsubscript{5}O\textsubscript{10}
- [M+Na]^+ 768.3630 m/z (measured), 768.2282 m/z (calculated): C\textsubscript{40}H\textsubscript{35}N\textsubscript{5}O\textsubscript{10}Na
- [M+K]^+ 784.3323 m/z (measured), 784.2021 m/z (calculated): C\textsubscript{40}H\textsubscript{35}N\textsubscript{5}O\textsubscript{10}K

IR: ν = 3439, 1612, 1529, 1115, 955, 621, 491 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, DMSO): δ =16.34 (s, 5 H, O\textsubscript{H}), 9.26 (s, 5 H, H\textsubscript{C}=N), 7.53 (s, 5 H, Ar-\textit{H}), 7.51 (s, 5 H, Ar-\textit{H}), 3.84 (s, 15 H, CH\textsubscript{3})

Due to the even lower solubility of the product in DMSO than one of \textit{p}-(\textit{tert}-butyl)-campestarene, \textsuperscript{13}C NMR spectrum was not carried out.
Penta-ethylpropanoate(oxy)-campestarene, **Cam-4 (NEW)**

![Chemical Structure Image]

**General Method D.**

Ethyl 2-(3-formyl-4-hydroxy-5-nitrophenoxo)propanoate, **C-17** (0.251 g, 0.886 mmol) in EtOH (20.0 mL) and water (3.00 mL). Purified twice by flash alumina column chromatography (elucent: 3-10% MeOH in DCM). By-products washed with 3% MeOH in DCM and the pure purple product was collected with 4-10% MeOH in DCM Yield: 90.0 mg, 43%.

**MALDI-TOF-MS**

[M+H]$^+$ 1176.45 m/z (measured), 1176.43 m/z (calculated): C$_{60}$H$_{56}$N$_{5}$O$_{20}$

[M+Na]$^+$ 1198.45 m/z (measured), 1198.41 m/z (calculated): C$_{60}$H$_{58}$N$_{5}$O$_{20}$Na

[M+K]$^+$ 1214.43 m/z (measured), 1214.39 m/z (calculated): C$_{60}$H$_{58}$N$_{5}$O$_{20}$K

$^1$H NMR (500 MHz, DMSO): $\delta$ =16.51 (s, 5 H, $OH$), 9.27 (s, 5 H, $HC=N$), 7.67 (s, 5 H, Ar-$H$), 7.06 (s, 5 H, Ar-$H$), 5.01 (q, 5 H, $^3J = 6.7$ Hz, $HI$), 4.22 (q, 10 H, $^3J = 6.7$ Hz, $H4$), 1.57 (d, 15 H, $^3J = 6.7$ Hz, $H2$), 1.23 (t, 15 H, $^3J = 6.7$ Hz, $H5$)

The solubility of the compound was too poor to obtain a $^{13}$C NMR spectrum, even after 100,000 scans.
Pentaaceto-campestarene, **Cam-5 (NEW)**

![Chemical Structure](image)

**General Method D.**

2-(3-formyl-4-hydroxy-5-nitrophenoxyl)acetic acid, **C-18** (0.020 g, 0.083 mmol), EtOH (2.00 mL) and water (0.300 mL). Purification: After addition of water (10.0 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was re-dissolved in 0.1 M NaOH (1.00 mL) and purified by Sephadex G-10 column chromatography. The collected purple solution was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 2.00 mg, 13%

**MALDI-TOF-MS**

[M-H]$^-$ 964.27 m/z (measured), 964.18 m/z (calculated): $C_{45}H_{34}N_5O_{20}$

[M+Na-2H]$^-$ 986.26 m/z (measured), 986.16 m/z (calculated): $C_{45}H_{33}N_5O_{20}Na$

[M+K-2H]$^-$ 1002.26 m/z (measured), 1002.14 m/z (calculated): $C_{45}H_{33}N_5O_{20}K$

$^1$H NMR (300 MHz, DMSO): $\delta = 16.39$ (s, 5 H, **OH**), 9.31 (s, 5 H, **H**C=N), 7.66 (s, 5 H, **Ar**-H), 7.12 (s, 5 H, **Ar**-H), 4.75 (s, 10 H, **HI**)

Due to the low solubility of the product in DMSO, $^{13}$C NMR spectrum was not carried out.
Pentapropionoxy-campestarene, *Cam-6* (NEW)

![Chemical Structure](image)

**General Method D.**

2-(3-formyl-4-hydroxy-5-nitrophenoxy)propanoic acid, *C-19* (0.320 g, 1.26 mmol) in EtOH (35.0 mL) and water (4.00 mL). Purification: After addition of water (20.0 mL), the mixture was acidified with 0.1 M HCl to give purple precipitate which was re-dissolved in 0.1 M NaOH (1.00 mL) and purified by Sephadex G-10 column chromatography. The collected purple solution was acidified with 0.1 M HCl to give purple precipitate which was collected by centrifuge, washed with minimum amount of water and dried under vacuum to give purple solid products. Yield: 28.0 mg, 11%

**MALDI-TOF-MS**

[M+H]$^+$ 1036.28 m/z (measured), 1036.27 m/z (calculated): C$_{50}$H$_{46}$N$_5$O$_{20}$

[M+Na]$^+$ 1058.25 m/z (measured), 1058.26 m/z (calculated): C$_{50}$H$_{45}$N$_5$O$_{20}$Na

[M+K]$^+$ 1074.23 m/z (measured), 1074.23 m/z (calculated): C$_{50}$H$_{45}$N$_5$O$_{20}$K

$^1$H NMR (400 MHz, DMSO): $\delta$ =16.49 (s, 5 H, $OH$), 9.30 (s, 5 H, $HC=\text{N}$), 7.66 (s, 5 H, Ar-$H$), 7.06 (s, 5 H, Ar-$H$), 4.90 (d, 5 H, $^3J = 7.0$ Hz, $HI$), 1.57 (d, 15 H, $^3J = 7.0$ Hz, $H2$)

The solubility of the compound was too poor to obtain a $^{13}$C NMR spectrum, even after 100,000 scans.
Singapore Pentamers

**General Method F.**\(^{35, 63g}\) Two equivalents of POCl\(_3\) was added to a solution of the corresponding amino-benzoic acid in MeCN at r.t. The mixture was stirred vigorously for 10 min. 3 equivalents of Et\(_3\)N was added to the reaction mixture which was stirred overnight at r.t. After removal of the solvent, the residue was purified by flash column chromatography.

**General Method G.**\(^{35, 63g}\) Three and half equivalents of Methyl iodide was added to a solution of the corresponding methyl hydroxy-nitrobenzoate and 4 equivalents of K\(_2\)CO\(_3\) in DMF. The reaction mixture was heated at 50 °C overnight, the solvent removed under vacuum, redissolved in DCM, washed with water, dried over MgSO\(_4\) and the solvent removed under vacuum.

**General Method H.**\(^{35, 63g}\) The corresponding methyl methoxy-nitrobenzoate was completely dissolved in hot MeOH. 2 equivalents of 1 M NaOH was added to the solution. The reaction mixture was refluxed for 2 h, the solvent removed under vacuum, quenched with water and neutralised by addition of 1 M HCl until the pH reached 1. A white solid precipitated. The crude product was filtered, washed with water and the solvent removed under vacuum. The product can be used for the further reaction without purification.

**General Method I.**\(^{35, 58b, 63g}\) A mixture of the corresponding methoxy-nitrobenzoic acid and Pd/C (10% in mass) in THF or MeOH was added into a hydrogenation vessel and the nitro group was reduced at 40 °C and 450 kPa for 18 h. Filtration and removal of the solvent gave a product.

**General Method J.**\(^{63g}\) Two equivalents of K\(_2\)CO\(_3\) and 1 equivalent of the corresponding alkyl halide were added to a solution of methyl 2,5-dihydroxybenzoate, \(\text{S-6}\) in dry acetone. The reaction mixture was refluxed for 48 h, cooled to r.t. and filtered. The filtrate was evaporated under vacuum, redissolved in DCM, washed with water, dried over Na\(_2\)SO\(_4\) and the solvent removed under vacuum to give a crude product.

**General Method K.**\(^{63g}\) A mixture of methyl hydroxy-benzoate substituted with the corresponding alkoxy group, Montmorillonite K 10 (0.500 g/mol) and 1 equivalent of bismuth nitrate in THF was stirred at r.t. for 1 h. After filtration, the filtrate was evaporated under vacuum, redissolved in DCM, washed with 1 M HCl and water, dried over Na\(_2\)SO\(_4\) and the solvent removed under vacuum.
Methyl 2,5-dihydroxybenzoate, S-1

Conc. H₂SO₄ (5.00 mL) was added to a solution of 2,5-dihydroxybenzoic acid (4.62 g, 30.0 mmol) in MeOH (60.0 mL). The reaction mixture was refluxed for 48 h, cooled to r.t., the solvent removed under vacuum, redissolved in DCM (100 mL), washed with water (50.0 mL x 2), dried over Na₂SO₄ and the solvent removed under vacuum to give a yellow oil which was solidified at r.t. Yield: 4.19 g, 83%

HRMS (ESI)
[M+H]⁺ 169.0497 m/z (measured), 169.0495 m/z (calculated): C₈H₉O₄
[M+Na]⁺ 191.0315 m/z (measured), 191.0315 m/z (calculated): C₈H₈O₄Na

¹H NMR (400 MHz, CDCl₃): δ = 10.35 (s, 1 H, Ha), 7.28 (d, 1 H, ⁴J = 3.2 Hz, H₅), 7.03 (dd, 1 H, ⁴J = 3.2 Hz, H₃), 6.89 (d, 1 H, ³J = 8.8 Hz, H₂), 5.11 (s, 1 H, Hb), 3.93 (s, 3 H, H₈)

¹³C NMR (100 MHz, CDCl₃): δ = 170.18 (C₇), 155.71 (C₁), 147.78 (C₄), 124.13 (C₃), 118.50 (C₂), 114.79 (C₅), 112.19 (C₆), 52.38 (C₈)
Methyl 2-hydroxy-5-methoxybenzoate, S-2

General Method J.
Methyl iodide (0.490 mL, 8.00 mmol), dry acetone (30.0 mL) and DCM (100 mL). Purified by flash column chromatography (eluent- EtOAc : n-hexane = 1:4) to give a yellow oil. Yield: 1.13 g, 78%

HRMS (ESI)
[M+H]$^+$ 183.0657 m/z (measured), 183.0652 m/z (calculated): C$_9$H$_{11}$O$_4$
[M+Na]$^+$ 205.0478 m/z (measured), 205.0471 m/z (calculated): C$_{9}$H$_{10}$O$_4$Na
GC-MS: 182.1 m/z (measured), 182.1 m/z (calculated): C$_9$H$_{10}$O$_4$

$^1$H NMR (400 MHz, CDCl$_3$): δ = 10.36 (s, 1 H, $H_a$), 7.29 (d, 1 H, $^4J = 3.1$ Hz, $H_5$), 7.10 (dd, 1 H, $^4J = 3.1$ Hz, $H_3$), 6.93 (d, 1 H, $^3J = 9.0$ Hz, $H_2$), 3.95 (s, 1 H, $H_8$), 3.78 (s, 3 H, $H_9$)

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 170.43 ($C_7$), 156.21 ($C_1$), 152.15 ($C_4$), 124.21 ($C_3$), 118.69 ($C_2$), 111.98 ($C_5$), 56.00 ($C_9$), 52.44 ($C_8$)
Methyl 2-hydroxy-5-(octyloxy)benzoate, S-3

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\]

General Method J.
1-bromooctane (1.38 mL, 8.00 mmol), acetone (30.0 mL) and DCM (100 mL). Recrystallized from MeOH. Yield of the crude product: 2.07 g, 93%

HRMS (ESI)
[M+H]^+ 281.1734 m/z (measured), 281.1747 m/z (calculated): C_{16}H_{25}O_4
[M+Na]^+ 303.1559 m/z (measured), 303.1567 m/z (calculated): C_{16}H_{24}O_4Na
GC-MS: 280.1 m/z (measured), 280.1 m/z (calculated): C_{16}H_{24}O_4

^1H NMR (300 MHz, CDCl_3): δ = 10.33 (s, 1 H, H_a), 7.29 (d, 1 H, J = 3.1 Hz, H_5), 7.09 (dd, 1 H, J = 3.1 Hz, H_3), 6.91 (d, 1 H, J = 9.0 Hz, H_2), 3.94 (s, 3 H, H_8), 3.92 (t, 2 H, J = 6.6 Hz, H_9), 1.8-1.7 (m, 2 H, H^*), 1.4-1.2 (m, 10 H, H^*), 0.90 (t, 3 H, J = 7.0 Hz, H_10)

^13C NMR (75 MHz, CDCl_3): δ = 170.49 (C_7), 156.08 (C_1), 151.70 (C_4), 124.73 (C_3), 118.58 (C_2), 113.05 (C_5), 112.00 (C_6), 68.99 (C_9), 52.44 (C_8), 31.95, 29.49, 29.43, 29.37, 26.17, 22.79 (C^*), 14.22 (C_{10})
Methyl 5-(benzoyloxy)-2-hydroxybenzoate, **S-4**

![Chemical structure](image)

**General Method J.**\(^{63a}\)

Benzyl bromide (0.350 mL, 3.00 mmol) in a solvent mixture of CHCl\(_3\) (16.0 mL) and MeOH (8.00 mL) instead of acetone. DCM (50.0 mL). Purified by flash silica column chromatography (eluent-DCM) to give a yellow oil which was recrystallised from n-hexane. Yield: 0.310 g, 40%

HRMS (ESI)

[M+H]\(^+\) 259.0969 m/z (measured), 259.0965 m/z (calculated): C\(_{15}\)H\(_{15}\)O\(_4\)

[M+Na]\(^+\) 281.0791 m/z (measured), 281.0784 m/z (calculated): C\(_{15}\)H\(_{14}\)O\(_4\)Na

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 10.37\) (s, 1 H, \(Ha\)), 7.45-7.33 (m, 6 H, \(H5, 11, 12, 13\)), 7.17 (dd, 1 H, \(J = 3.1\) Hz, \(H3\)), 6.94 (d, 1 H, \(J = 9.1\) Hz, \(H2\)), 5.02 (s, 2 H, \(H9\)), 3.94 (s, 3 H, \(H8\))

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 170.39\) (C7), 156.42 (C4), 151.30 (C1), 136.96 (C10), 128.73 (C12), 128.19 (C13), 127.70 (C11), 124.96 (C3), 118.70 (C5), 113.67 (C6), 112.08 (C6), 71.03 (C9), 52.46 (C8)
Methyl 2-hydroxy-3-nitrobenzoate, S-5

\[
\begin{align*}
\text{O}_3\text{N} & \\
2 & \text{OH} \\
1 & \text{O} \\
7 & \text{O} \\
8 & \\
3 & \\
4 & \\
5 & \\
6 & \\
\end{align*}
\]

Conc. HNO\textsubscript{3} (6.05 mL, 94.2 mmol, 69\%), was added to salicylic acid (10.0 g, 72.5 mmol) in DCM (200 mL) at 0 °C with stirring, followed by dropwise addition of conc. H\textsubscript{2}SO\textsubscript{4} (10.6 mL, 145 mmol). After 20 min stirring at 0 °C, the reaction mixture was poured into water (500 mL), filtered and redissolved in MeOH (250 mL). After addition of conc. H\textsubscript{2}SO\textsubscript{4} (21.9 mL, 388 mmol), the reaction mixture was refluxed for 48 h, the solvent removed under vacuum, redissolved in DCM (200 mL), washed with water (100 mL x 2) and saturated aqueous NaHCO\textsubscript{3} (100 mL), dried over MgSO\textsubscript{4} and the solvent removed under vacuum to give a crude product which was purified by flash column chromatography (eluent- DCM : n-hexane = 1:4). The first fraction was the unwanted para-product and the second fraction was the pure product. Yield: 2.98 g, 21%

HRMS (ESI)
[M+Na]\textsuperscript{+} 220.0217 m/z (measured), 220.0216 m/z (calculated): C\textsubscript{8}H\textsubscript{7}NO\textsubscript{5}Na

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 11.97 \text{ (s, 1 H, } H_a)\), 8.14 (m, 2 H, \(H_3\text{ and } H_5\)), 7.02 (t, 1 H, \(^J = 8.0 \text{ Hz, } H_4\)), 4.01 (s, 3 H, \(H_8\))
Methyl 3-amino-2-methoxybenzoate, S-5a

General Method I.
Methyl 2-methoxy-3-nitrobenzoate, S-5 (1.00 g, 4.74 mmol) and THF (50.0 mL). A yellow oil product. Yield: 0.853 g, 99%.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.20$ (dd, 1 H, $^4J = 2.0$ Hz, H$_5$), 6.97 (t, 1 H, $^3J = 7.7$ Hz, H$_4$), 6.91 (dd, 1 H, $^4J = 2.0$ Hz, H$_3$), 3.90 (s, 3 H, H$_9$), 3.85 (s, 3 H, H$_8$)
Methyl 2-hydroxy-5-methoxy-3-nitrobenzoate, S-6

![Chemical structure of S-6](image)

**General Method K.**

Methyl 2-hydroxy-5-methoxybenzoate, S-2 (0.180 g, 1 mmol), THF (5.00 mL) and DCM (50.0 mL). A yellow solid product. Yield: 0.15 g, 67%

HRMS (ESI)

[M+H]⁺ 228.0509 m/z (measured), 228.0503 m/z (calculated): C₉H₁₀NO₆

[M+Na]⁺ 250.0331 m/z (measured), 250.0329 m/z (calculated): C₉H₁₀NO₆Na

[M+K]⁺ 266.0071 m/z (measured), 266.0061 m/z (calculated): C₉H₁₀NO₆K

GC-MS: 227.0 m/z (measured), 227.0 m/z (calculated): C₉H₈NO₆

¹H NMR (300 MHz, CDCl₃): δ = 11.45 (s, 1 H, Ha), 7.73 (d, 1 H, ⁴J = 3.3 Hz, H₃), 7.69 (d, 1 H, ⁴J = 3.3 Hz, H₅), 4.00 (s, 3 H, H₈), 3.84 (s, 1 H, H₉)

¹³C NMR (75 MHz, CDCl₃): δ = 170.64 (C₇), 150.87 (C₁), 150.04 (C₄), 142.41 (C₂), 122.05 (C₅), 116.54 (C₃), 56.44 (C₉), 53.30 (C₈)
Methyl 2-hydroxy-3-nitro-5-(octyloxy)benzoate, S-7

\[ \text{O}_2\text{N} \]
\[ \begin{array}{c}

1 \\
OH \\
2 \\
\text{O} \\
3 \\
\text{O} \\
4 \\
5 \\
6 \\
7 \\
8 \\
9 \\
10
\end{array} \]

General Method K.

Methyl 2-hydroxy-5-(octyloxy)benzoate, S-3 (2.10 g, 7.5 mmol), THF (100 mL) and DCM (250 mL).

An orange crude product which can be recrystallized from MeOH. Yield of the crude product: 1.27 g, 52%

HRMS (ESI)

[M+H]\(^+\) 326.1586 m/z (measured), 326.1598 m/z (calculated): C\(_{16}\)H\(_{24}\)NO\(_6\)

[M+Na]\(^+\) 348.1412 m/z (measured), 348.1422 m/z (calculated): C\(_{16}\)H\(_{23}\)NO\(_6\)Na

[M+K]\(^+\) 364.1149 m/z (measured), 364.1157 m/z (calculated): C\(_{16}\)H\(_{23}\)NO\(_6\)K

GC-MS: 325.2 m/z (measured), 325.2 m/z (calculated): C\(_{16}\)H\(_{23}\)NO\(_6\)

\(^1\)H NMR (300 MHz, CDCl\(_3\), \(\delta = 11.44\) (s, \(1\) H, \(\text{Ha}\)), 7.72 (d, \(1\) H, \(^4J = 3.2\) Hz, \(\text{H3}\)), 7.69 (d, \(1\) H, \(^4J = 3.2\) Hz, \(\text{H5}\)), 4.00 (s, \(3\) H, \(\text{H8}\)), 3.98 (t, \(2\) H, \(^3J = 6.5\) Hz, \(\text{H9}\)), 1.8-1.7 (m, \(2\) H, \(\text{H*}\)), 1.4-1.2 (m, \(10\) H, \(\text{H*}\)), 0.91 (t, \(3\) H, \(^3J = 6.9\) Hz, \(\text{H10}\))

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 168.76\) (\(\text{C7}\)), 150.44 (\(\text{C1}\)), 149.92 (\(\text{C4}\)), 138.90 (\(\text{C2}\)), 122.73 (\(\text{C5}\)), 117.11 (\(\text{C3}\)), 116.53 (\(\text{C6}\)), 69.49 (\(\text{C9}\)), 53.25 (\(\text{C8}\)), 31.92, 29.41, 29.34, 29.17, 26.06, 22.79 (\(\text{C*}\)), 14.22 (\(\text{C10}\))
Methyl 5-(benzyloxy)-2-hydroxy-3-nitrobenzoate, **S-8** (NEW)

![Chemical structure](image)

**General Method K.**

Methyl 5-(benzyloxy)-2-hydroxy-3-nitrobenzoate, **S-4** (0.310 g, 1.2 mmol), THF (20.0 mL) and DCM (150 mL). A yellow oil which was recrystallised from ice-cold MeOH. Yield: 0.110 g, 31%

**HRMS (ESI)**

[M+H]$^+$ 304.0818 m/z (measured), 304.0816 m/z (calculated): C$_{15}$H$_{14}$NO$_6$

[M+Na]$^+$ 326.0626 m/z (measured), 326.0635 m/z (calculated): C$_{15}$H$_{13}$NO$_6$Na

[M+K]$^+$ 342.0371 m/z (measured), 342.0374 m/z (calculated): C$_{15}$H$_{13}$NO$_6$K

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 11.48 (s, 1 H, $H_a$), 7.81 (d, 1 H, $^4J = 3.3$ Hz, $H_3$), 7.78 (d, 1 H, $^4J = 3.3$ Hz, $H_5$), 7.41-7.35 (m, 5 H, $H_{11, 12, 13}$), 5.07 (s, 2 H, $H_9$), 3.99 (s, 3 H, $H_8$)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 168.69 ($C_7$), 150.25 ($C_1$), 149.85 ($C_4$), 137.71 ($C_2$), 135.68 ($C_{10}$), 128.92 ($C_{12}$), 128.64 ($C_{13}$), 127.75 ($C_{11}$), 123.12 ($C_5$), 117.69 ($C_3$), 116.56 ($C_6$), 71.40 ($C_9$), 53.30 ($C_8$)
Methyl 2-methoxy-3-nitrobenzoate, **S-9**

![Chemical Structure](image)

**General Method G.**
Methyl 2-hydroxy-3-nitrobenzoate, **S-5** (3.00 g, 15.2 mmol) and DMF (60.0 mL). A yellow/white solid product. Yield: 1.84 g, 58%

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.95$ (dd, 1 H, $^4J = 1.8$ Hz, $H3$), 7.83 (dd, 1 H, $^4J = 1.8$ Hz, $H5$), 7.21 (t, 1 H, $^3J = 8.0$ Hz, $H4$), 3.92 (s, 3 H, $H9$), 3.87 (s, 3 H, $H8$)
Methyl 2,5-dimethoxy-3-nitrobenzoate, S-10

General Method G.
Methyl 2-hydroxy-5-methoxy-3-nitrobenzoate, S-6 (0.780 g, 3.43 mmol), DMF (10.0 mL) and DCM (50.0 mL). A dark-brown oil product which was solidified in 30 min. Yield: 0.720 g, 86%

HRMS (ESI)
[M+H]^+ 242.0654 m/z (measured), 242.0659 m/z (calculated): C_{10}H_{12}NO_{6}
[M+Na]^+ 264.0480 m/z (measured), 264.0479 m/z (calculated): C_{10}H_{11}NO_{6}Na
[M+K]^+ 280.0219 m/z (measured), 280.0218 m/z (calculated): C_{10}H_{11}NO_{6}K
GC-MS: 241.1 m/z (measured), 241.1 m/z (calculated): C_{10}H_{11}NO_{6}

^1H NMR (300 MHz, CDCl₃) δ = 7.55 (d, 1 H, ^4J = 3.3 Hz, H3), 7.43 (d, 1 H, ^4J = 3.3 Hz, H5), 3.95 (s, 3 H, H9 or H10), 3.94 (s, 3 H, H9 or H10), 3.86 (s, 3 H, H8)

^13C NMR (75 MHz, CDCl₃): δ = 164.87 (C7), 154.88 (C2), 147.20 (C4), 146.03 (C1), 128.26 (C6), 121.15 (C5), 113.69 (C3), 64.51 (C9 or C10), 56.38 (C8), 52.97 (C9 or C10)
Methyl 2-methoxy-3-nitro-5-(octyloxy)benzoate, S-11

General Method G.

Methyl 2-hydroxy-3-nitro-5-(octyloxy)benzoate, S-7 (0.550 g, 1.71 mmol), DMF (5.00 mL) and DCM (25.0 mL). A yellow oil product which can be recrystallized from MeOH. Yield of the crude product: 0.348 g, 60%

HRMS (ESI)

[M+H]^+ 340.1748 m/z (measured), 340.1755 m/z (calculated): C_{17}H_{26}NO_6
[M+Na]^+ 362.1563 m/z (measured), 362.1574 m/z (calculated): C_{17}H_{25}NO_6Na
[M+K]^+ 378.1304 m/z (measured), 378.1313 m/z (calculated): C_{17}H_{25}NO_6K

GC-MS: 339.2 m/z (measured), 339.2 m/z (calculated): C_{17}H_{25}NO_6

^1H NMR (300 MHz, CDCl_3) δ = 7.52 (d, 1 H, 4^J = 3.2 Hz, H_3), 7.40 (d, 1 H, 4^J = 3.2 Hz, H_5), 3.98 (t, 2 H, 3^J = 6.5 Hz, H_9), 3.93 (s, 3 H, H_8), 3.92 (s, 3 H, H_11), 1.8-1.7 (m, 2 H, H*), 1.4-1.2 (m, 10 H, H*), 0.89 (t, 3 H, 3^J = 7.0 Hz, H_{10})

^13C NMR (75 MHz, CDCl_3): δ = 164.84 (C_7), 154.43 (C_2), 146.61 (C_4), 145.75 (C_1), 128.09 (C_6), 121.62 (C_5), 114.07 (C_3), 69.32 (C_9), 64.41 (C_8), 52.85 (C_{11}), 31.86, 29.33, 29.27, 29.04, 25.98, 22.73 (C*), 14.16 (C_{10})
Methyl 5-(benzyloxy)-2-methoxy-3-nitrobenzoate, **S-12** (NEW)

![Chemical structure](image)

**General Method G.**
Methyl 5-(benzyloxy)-2-hydroxy-3-nitrobenzoate, **S-8** (0.070 g, 0.23 mmol), dry DMF (2.00 mL) and DCM (20.0 mL). A dark-brown oil. Yield: 0.072 g, 99%.

HRMS (ESI)
[M+H]$^+$ 318.0956 m/z (measured), 318.0972 m/z (calculated): C_{16}H_{16}NO_{6}
[M+Na]$^+$ 340.0781 m/z (measured), 340.0792 m/z (calculated): C_{16}H_{15}NO_{6}Na
[M+K]$^+$ 356.0520 m/z (measured), 356.0531 m/z (calculated): C_{16}H_{15}NO_{6}K

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.65 (d, 1 H, $^4$J = 3.2 Hz, H$_5$), 7.52 (d, 1 H, $^4$J = 3.2 Hz, H$_3$), 7.42-7.35 (m, 5 H, H$_{11, 12, 13}$), 5.09 (s, 2 H, H$_9$), 3.95 (s, 6 H, H$_8$, Ha)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 164.49 (C$_7$), 153.73 (C$_4$), 146.81 (C$_1$), 145.59 (C$_2$), 135.38 (C$_{10}$), 128.69 (C$_{12}$), 128.42 (C$_{13}$), 128.01 (C$_6$), 127.52 (C$_{11}$), 121.86 (C$_5$), 114.38 (C$_3$), 70.97 (C$_9$), 64.24 (C$_a$), 52.72 (C$_8$)
2-Methoxy-3-nitrobenzoic acid, S-13

General Method H.
Methyl 2-methoxy-3-nitrobenzoate, S-9 (2.00 g, 9.5 mmol) and MeOH (30.0 mL). Yield: 1.05 g, 56%

HRMS (ESI)  
[M-H]⁻ 196.0254 m/z (measured), 196.0251 m/z (calculated): C₈H₆NO₅

¹H NMR (300 MHz, CDCl₃): δ = 8.28 (dd, 1 H, ⁴J = 1.8 Hz, H₃ or H₅), 8.04 (dd, 1 H, ⁴J = 1.8 Hz, H₃ or H₅), 7.38 (t, 1 H, ³J = 8.0 Hz, H₄), 4.07 (s, 3 H, H₈)
2,5-Dimethoxy-3-nitrobenzoic acid, **S-14**

![Chemical structure of 2,5-dimethoxy-3-nitrobenzoic acid](image)

**General Method H.**
Methyl 2,5-dimethoxy-3-nitrobenzoate, **S-10** (0.715 g, 2.96 mmol) and MeOH (60.0 mL). Light brown precipitate. Yield: 0.600 g, 90%

HRMS (ESI)
[M+H]^+ 228.0509 m/z (measured), 228.0503 m/z (calculated): C_9H_{10}NO_6
[M+Na]^+ 250.0331 m/z (measured), 250.0329 m/z (calculated): C_9H_{10}NO_6Na
[M+K]^+ 266.0071 m/z (measured), 266.0061 m/z (calculated): C_9H_{10}NO_6K
GC-MS: 227.0 m/z (measured), 227.0 m/z (calculated): C_9H_{10}NO_6

^1H NMR (300 MHz, CDCl₃) δ = 7.81 (d, 1 H, ^4J = 3.4 Hz, H3), 7.58 (d, 1 H, ^4J = 3.4 Hz, H5), 4.03 (s, 3 H, H9), 3.89 (s, 3 H, H8)

^13C NMR (75 MHz, CDCl₃): δ = 165.08 (C7), 15.82 (C2), 145.44 (C4), 145.04 (C1), 125.96 (C6), 121.83 (C5), 116.00 (C3), 65.01 (C8 or C9), 56.54 (C8 or C9)
2-Methoxy-3-nitro-5-(octyloxy)benzoic acid, S-15

General Method H.
Methyl 2-methoxy-3-nitro-5-(octyloxy)benzoate, S-11 (0.348 g, 1.02 mmol) and MeOH (30.0 mL).
Light brown precipitate. Yield: 0.300 g, 90%

HRMS (ESI)
[M+H]$^+$ 326.1602 m/z (measured), 326.1598 m/z (calculated): C\textsubscript{16}H\textsubscript{24}NO\textsubscript{6}
[M+Na]$^+$ 348.1427 m/z (measured), 348.1428 m/z (calculated): C\textsubscript{16}H\textsubscript{23}NO\textsubscript{6}Na
[M+K]$^+$ 364.1164 m/z (measured), 364.1157 m/z (calculated): C\textsubscript{16}H\textsubscript{23}NO\textsubscript{6}K
GC-MS: 325.1 m/z (measured), 325.1 m/z (calculated): C\textsubscript{16}H\textsubscript{23}NO\textsubscript{6}

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ = 7.79 (t, 1 H, \textsuperscript{4}J = 3.0 Hz, H3), 7.56 (t, 1 H, \textsuperscript{4}J = 3.0 Hz, H5), 4.03 (t, 2 H, \textsuperscript{3}J = 6.5 Hz, H8) 4.02 (s, 3 H, H10), 1.8-1.7 (m, 2 H, H*), 1.4-1.2 (m, 10 H, H*), 0.89 (t, 3 H, \textsuperscript{3}J = 7.1 Hz, H9)

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ = 165.79 (C7), 155.05 (C2), 146.57 (C4), 144.90 (C1), 125.88 (C6), 122.35 (C5), 116.29 (C3), 69.57 (C8), 64.96 (C10), 31.86, 29.33, 29.27, 29.04, 25.98, 22.73 (C*), 14.16 (C9)
5-(benzylxoy)-2-Methoxy-3-nitrobenzoic acid, S-16* (NEW)

![Chemical Structure Image]

**General Method H.**

Methyl 5-(benzylxoy)-2-methoxy-3-nitrobenzoate, S-12 (0.073 g, 0.23 mmol) and MeOH (4.00 mL). Creamy yellow precipitate. Yield: 0.069 g, 99%.

HRMS (ESI) 
[M+Na]^+ 326.0626 m/z (measured), 326.0635 m/z (calculated): C_{15}H_{13}NO_{6}Na

$^1$H NMR (300 MHz, CDCl$_3$): δ = 7.88 (d, 1 H, $^4$J = 3.2 Hz, H5), 7.64 (d, 1 H, $^4$J = 3.2 Hz, H3), 7.43-7.35 (m, 5 H, H11, 12, 13), 5.13 (s, 2 H, H9), 4.02 (s, 3 H, Ha)

$^{13}$C NMR (75 MHz, CDCl$_3$): δ = 166.45 (C7), 154.40 (C4), 147.19 (C1), 145.16 (C2), 135.25 (C10), 129.00 (C12), 128.79 (C13), 127.75 (C11), 126.07 (C6), 122.76 (C5), 116.71 (C3), 71.33 (C9), 64.94 (Ca)
3-Amino-2-methoxybenzoic acid, **S-17**

![Chemical Structure](attachment:image.png)

**General Method I.**

A mixture of 2-methoxy-3-nitrobenzoic acid, **S-13** (0.500 g, 2.53 mmol) and THF (15.0 mL). A brown oil product. Yield: 0.419 g, 99%.

HRMS (ESI)

[M+H]$^+$ 168.0656 m/z (measured), 168.0655 m/z (calculated): C₈H₁₀NO₃

[M+Na]$^+$ 190.0478 m/z (measured), 190.0475 m/z (calculated): C₈H₉NO₃Na

$^1$H NMR (300 MHz, CDCl₃): $\delta$ = 7.48 (dd, 1 H, $^4J = 1.8$ Hz, H₅), 7.08 (t, 1 H, $^3J = 7.9$ Hz, H₄), 6.99 (dd, 1 H, $^4J = 1.8$ Hz, H₃), 3.93 (s, 3 H, H₈)
3-Amino-2,5-dimethoxybenzoic acid, **S-18**

![Chemical structure of 3-Amino-2,5-dimethoxybenzoic acid](image)

**General Method I.**

2,5-dimethoxy-3-nitrobenzoic acid, **S-14** (0.600 g, 2.64 mmol) and MeOH (30.0 mL). A brown oil product. Yield: 0.513 g, 99%.

HRMS (ESI)

[M+H]^+ 198.0763 m/z (measured), 198.0761 m/z (calculated): C₉H₁₂NO₄

[M+Na]^+ 220.0591 m/z (measured), 220.0588 m/z (calculated): C₉H₁₁NO₄Na

[M+K]^+ 236.0324 m/z (measured), 236.0320 m/z (calculated): C₉H₁₁NO₄K

GC-MS: 197.1 m/z (measured), 197.1 m/z (calculated): C₉H₁₁NO₄

¹H NMR (400 MHz, CDCl₃): δ = 7.00 (d, 1 H, 4J = 3.0 Hz, H₅), 6.53 (d, 1 H, 4J = 3.0 Hz, H₃), 3.90 (s, 3 H, H⁹), 3.78 (s, 3 H, H⁸)
3-Amino-2-methoxy-5-(octyloxy)benzoic acid, S-19

2-methoxy-3-nitro-5-(octyloxy)benzoic acid, S-15 (0.300 g, 0.90 mmol) and MeOH (20.0 mL). A brown oil product. Yield: 0.259 g, 97%.

HRMS (ESI)
[M+H]+ 296.1846 m/z (measured), 296.1856 m/z (calculated): C₁₆H₂₆NO₄
[M+Na]+ 318.1661 m/z (measured), 318.1676 m/z (calculated): C₁₆H₂₅NO₄Na
[M+K]+ 334.1406 m/z (measured), 334.1415 m/z (calculated): C₁₆H₂₅NO₄K
GC-MS: 295.1 m/z (measured), 295.1 m/z (calculated): C₁₆H₂₅NO₄

¹H NMR (400 MHz, CDCl₃): δ = 6.97 (d, 1 H, 4J = 3.0 Hz, H5), 6.52 (d, 1 H, 4J = 3.0 Hz, H3), 3.93 (t, 2 H, 3J = 6.5 Hz, H8), 3.88 (s, 3 H, H10), 1.7 (m, 2 H, H*), 1.4-1.2 (m, 10 H, H*), 0.89 (t, 3 H, 3J = 7.1 Hz, H9)
3-Amino-5-(benzylxoy)-2-methoxybenzoic acid, S-20* (NEW)

![Chemical structure of 3-Amino-5-(benzylxoy)-2-methoxybenzoic acid]

**General Method I.**

5-(benzyloxy)-2-methoxy-3-nitrobenzoic acid, S-16 (0.700 g, 2.3 mmol), MeOH (80.0 mL) and Pt/C (0.070 g, 10% in mass) instead of Pd/C. A red/brown sticky oil product. Yield: 0.608 g, 97%.

**HRMS (ESI)**

[M+H]$^+$ 274.1068 m/z (measured), 274.1074 m/z (calculated): C$_{15}$H$_{16}$NO$_4$

[M+Na]$^+$ 296.0885 m/z (measured), 296.0893 m/z (calculated): C$_{15}$H$_{15}$NO$_4$Na

$^1$H NMR (300 MHz, CDCl$_3$): δ = 7.40 - 7.37 (m, 5 H, H$_{11}$, I$_2$, I$_3$), 7.08 (d, 1 H, $^4$J = 2.8 Hz, H$_5$), 6.06 (d, 1 H, $^4$J = 2.8 Hz, H$_3$), 5.02 (s, 2 H, H$_8$), 3.88 (s, 3 H, H$_9$)

$^{13}$C NMR (75 MHz, DMSO): δ = 166.44 (C$_7$), 156.02 (C$_4$), 141.28 (C$_1$), 141.14 (C$_2$), 136.67 (C$_{10}$), 128.74, 128.22, 127.66 (C$_{11}$, I$_2$, I$_3$), 122.52 (C$_6$), 108.89 (C$_3$), 105.94 (C$_5$), 70.49 (C$_8$), 61.45 (C$_9$)
3-Amino-5-hydroxy-2-methoxybenzoic acid, S-21* (NEW)

![Chemical Structure](image)

**General Method I.**

5-(benzyloxy)-2-methoxy-3-nitrobenzoic acid, S-16 (0.600 g, 1.98 mmol) and MeOH (30.0 mL). A brown sticky oil product. Yield: 0.348 g, 96%.

HRMS (ESI)

[M+Na]^+ 206.0428 m/z (measured), 206.0424 m/z (calculated): C₈H₉NO₄Na

¹H NMR (500 MHz, DMSO): δ = 12.07 (s, 1 H, Ha), 9.00 (s, 1 H, H₈), 6.28 (d, 1 H, ⁴J = 2.9 Hz, H₃), 6.23 (d, 1 H, ⁴J = 2.9 Hz, H₅), 4.97 (s, 2 H, Hb), 3.59 (s, 3 H, H₉)

¹³C NMR (128 MHz, DMSO): δ = 167.64 (C₇), 153.15 (C₄), 142.99 (C₂), 138.47 (C₁), 125.81 (C₆), 104.83 (C₃), 103.48 (C₅), 60.07 (C₉)
3-Amino-2-fluorobenzoic acid, S-23

![Chemical Structure]

**General Method I.**

2-fluoro-3-nitrobenzoic acid (0.200 g, 1.08 mmol) and in MeOH (10.0 mL). Stirred at r.t. for 24 h under H₂ atmosphere using a balloon. A pink/people solid. Yield: 0.157 g, 94%.

HRMS (ESI)

[M+H]⁺ 156.0446 m/z (measured), 156.0455 m/z (calculated): C₇H₇FNO₂

[M+Na]⁺ 178.0274 m/z (measured), 178.0275 m/z (calculated): C₇H₆FNO₂Na

¹H NMR (400 MHz, DMSO): δ = 6.96 – 6.88 (m, 3 H, H1, 2, 3), 5.26 (s, 2 H, H1), 3.98 (s, 3 H, Ha)

¹³C NMR (100 MHz, DMSO): δ = 165.86, 148.00, 137.47, 137.34, 123.71, 123.67, 119.34, 119.29, 117.32
Methyl 2-fluoro-3-nitrobenzoate, **S-23a** \(^{59a}\)

![Chemical Structure](image)

Conc. H\(_2\)SO\(_4\) (2.00 mL) was added dropwise to 2-fluoro-3-nitrobenzoic acid (3.70 g, 20.0 mmol) in MeOH (40.0 mL) and the reaction mixture was heated at 60 °C for 2-3 h. After removal of the solvent, the residue was redissolved in DCM (200 mL) which was washed with water (100 mL x 2) and aqueous NaHCO\(_3\) (100 mL), dried over Na\(_2\)SO\(_4\) and the solvent removed under vacuum to give an orange solid. Yield: 3.37 g, 85%

HRMS (ESI)

\([\text{M+H}]^+\) 200.0353 m/z (measured), 200.0354 m/z (calculated): C\(_8\)H\(_7\)FNO\(_4\)

\([\text{M+Na}]^+\) 222.0176 m/z (measured), 222.0173 m/z (calculated): C\(_8\)H\(_6\)FNO\(_4\)Na

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.22 - 8.16 \) (m, 2 H, \(\text{H2, 3}\)), 7.40 (td, 1 H, \(^3\)J = 1.1 Hz, \(\text{H1}\)), 3.98 (s, 3 H, \(\text{H4}\))
Methyl 5-bromo-2-fluoro-3-nitrobenzoate, S-24\textsuperscript{59a}

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{Br} \\
\text{H}_2 & \quad \text{O} \\
\text{F} & \quad \text{3}
\end{align*}
\]

N-Bromosuccinimide (3.58 g, 20.2 mmol) was added to methyl 2-fluoro-3-nitrobenzoate, S-24 (3.34 g, 16.8 mmol) in conc. H\textsubscript{2}SO\textsubscript{4} (22.4 mL) / TFA (16.8 mL). The solution turned orange in colour. The reaction mixture was heated at 45 °C for 6 h and poured into ice-water to give white precipitate which was collected by filtration and recrystallized from MeOH to give colourless crystals. Yield: 3.90 g, 84%

HRMS (ESI)

\[\text{[M+Na]}^+ \text{ 299.9281 m/z (measured), 299.9278 m/z (calculated): C}_8\text{H}_5\text{BrFNO}_4\text{Na}\]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 8.33 - 8.29 \text{ (m, 2 H, H}_1, \text{ 2), 3.99 (s, 3 H, H}_3\text{)}\]

\(^{19}\text{F NMR (376 MHz, CDCl}_3\text{): } \delta = -118.02 \text{ (s, 1 F, F)}\]
Methyl 3'-(tert-butoxy)-4'-cyano-4-fluoro-5-nitro-[1,1'-biphenyl]-3-carboxylate, **S-25** (NEW)\textsuperscript{59a}

![Chemical Structure]

Methyl 5-bromo-2-fluoro-3-nitrobenzoate, **S-25** (0.421 g, 1.51 mmol), (3-(tert-butoxy)-4-cyanophenyl)boronic acid, **B-6** (0.398 g, 1.82 mmol) and potassium carbonate (0.628 g, 4.54 mmol) were dissolved/suspended in a mixture of toluene (12 mL) and water (4 mL). Tetrakis(triphenylphosphine)palladium(0) (0.088 g, 0.076 mmol) was added to the reaction mixture which was heated at 90 °C for 5 h. After cooled to r.t., the mixture was quenched with water (50.0 mL), extracted with DCM, dried over Na\textsubscript{2}SO\textsubscript{4} and the solvent removed under vacuum to give a black oil. The crude product was purified by flash silica chromatography (eluent: DCM) to give a yellow oil. Yield: 0.130 g, 23%

**HRMS (ESI)**

\[ [M+Na]^+ \text{m/z (measured), 395.1014 m/z (calculated): C}_{19}\text{H}_{17}\text{FN}_2\text{O}_5\text{Na} \]

\[ ^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 8.39 \text{ (dd, 1 H, } ^4\text{J} = 2.8 \text{ Hz, } H3\text{)}, 8.35 \text{ (dd, 1 H, } ^4\text{J} = 2.8 \text{ Hz, } H5\text{)}, 7.72 \text{ (d, 1 H, } ^3\text{J} = 7.9 \text{ Hz, } H12\text{)}, 7.36 \text{ (dd, 1 H, } ^4\text{J} = 1.7 \text{ Hz, } H13\text{)}, 7.32 \text{ (d, 1 H, } ^4\text{J} = 1.7 \text{ Hz, } H9\text{)}, 4.03 \text{ (s, 3 H, } H17\text{)}, 1.54 \text{ (s, 9 H, } H16\text{)} \]

\[ ^19\text{F NMR (470 MHz, CDCl}_3\text{): } \delta = -116.74 \text{ (s, 1 F, F)} \]

\[ ^{13}\text{C NMR (125 MHz, CDCl}_3\text{): } \delta = 163.03 \text{ (C1), 159.34 (C10), 155.78 (C7), 153.56 (C6), 142.15 (C8), 139.22 (C2), 136.01 (C4), 135.57 (C3), 134.48 (C12), 128.18 (C5), 121.83 (C13), 121.40 (C9), 116.80 (C14), 109.28 (C11), 83.40 (C15), 53.39 (C17), 29.08 (C16)} \]
Singapore Pentamer, **SP-1**

![Chemical Structure](image)

**General Method F.**

3-amino-2-methoxybenzoic acid, **S-5** (33.4 mg, 0.2 mmol) and MeCN (2.00 mL). Purified by flash silica column chromatography (eluent: EtOAc : DCM = 1:10). The first and third yellow fractions were impurities and the second fraction was the product as a white solid. Yield: 5.67 mg, 20%

**HRMS (ESI)**

[M+Na]$^+$ 768.2255 m/z (measured), 768.2276 m/z (calculated): C$_{40}$H$_{35}$N$_5$O$_{10}$Na

[M+K]$^+$ 784.1974 m/z (measured), 784.2016 m/z (calculated): C$_{40}$H$_{35}$N$_5$O$_{10}$K

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 10.87 (s, 5 H, Ha), 9.01 (dd, 5 H, $^4$J = 1.6 Hz, H5), 8.03 (dd, 5 H, $^4$J = 1.6 Hz, H3), 7.47 (t, 5 H, $^3$J = 8.0 Hz, H4), 4.09 (s, 15 H, H8)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 162.42 (C7), 146.65 (C1), 132.99 (C2), 126.71 (C4), 126.34 (C3), 125.77 (C6), 124.49 (C5), 63.45 (C8)
Pentamethoxypentamer, **SP-2**

![Chemical structure of SP-2](image)

**General Method F.**

3-amino-2,5-dimethoxybenzoic acid, **S-18** (0.125 g, 0.633 mmol) and MeCN (10.0 mL). Purified by flash silica column chromatography (eluent- EtOAc : DCM = 1:10). The first and third yellow fractions were impurities and the second fraction was the product as a white solid. Yield: 12.0 mg, 11%

**HRMS (ESI)**

[M+H]$^+ \ 896.2983 \text{ m/z (measured)}, 896.2985 \text{ m/z (calculated): } C_{45}H_{46}N_5O_{15}$

[M+Na]$^+ \ 918.2813 \text{ m/z (measured)}, 918.2804 \text{ m/z (calculated): } C_{45}H_{45}N_5O_{15}Na$

[M+K]$^+ \ 934.2528 \text{ m/z (measured)}, 934.2544 \text{ m/z (calculated): } C_{45}H_{45}N_5O_{15}K$

$^{1}$H NMR (400 MHz, CDCl$_3$): $\delta = 10.94 \text{ (s, 5 H, H10)}, 8.61 \text{ (d, 5 H, } J = 3.2 \text{ Hz, H5)}, 7.50 \text{ (d, 5 H, } J = 3.2 \text{ Hz, H3)}, 4.03 \text{ (s, 15 H, H7)}, 3.94 \text{ (s, 15 H, H8)}$
Pentaoctoxypentamer, SP-3

**General Method F.**

3-amino-2-methoxy-5-(octyloxy)benzoic acid, S-19 (0.140 g, 0.47 mmol) and MeCN (10.0 mL). Purified by flash silica column chromatography (eluent- EtOAc : DCM = 1:10). The first and third yellow fractions were impurities and the second fraction was the product as a white solid. Yield: 4.00 mg, 4 %

**HRMS (ESI)**

$[\text{M+H}]^+$ 1386.8435 m/z (measured), 1386.8462 m/z (calculated): C$_{80}$H$_{116}$N$_5$O$_{15}$

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 10.93$ (s, 5 H, $H_{10}$), 8.58 (d, 5 H, $^4J = 3.1$ Hz, $H_{5}$), 7.47 (d, 5 H, $^4J = 3.1$ Hz, $H_{3}$), 4.08 (t, 10 H, $^3J = 6.5$ Hz, $H_{8}$), 4.02 (s, 15 H, $H_{7}$), 1.84 – 1.25 (m, 60 H, $H^*$), 0.92 (t, 15 H, $^3J = 7.1$ Hz, $H_{11}$)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 162.33$ (C$_9$), 157.01 (C$_4$), 140.48 (C$_1$), 133.06 (C$_2$ or 6), 125.87 (C$_2$ or 6), 111.17 (C$_5$), 110.59 (C$_3$), 68.58 (C$_7$), 63.43 (C$_8$), 31.95, 29.82, 29.38, 29.32, 26.13 (C$_*$), 22.80 (C$_{12}$), 14.23 (C$_{11}$)
Pentabenzylxypentamer, SP-4*

General Method F.
3-amino-5-(benzylxy)-2-methoxybenzoic acid, S-20 (0.500 g, 1.83 mmol) and MeCN (20.0 mL). Purified by flash silica column chromatography (eluent - EtOAc : DCM = 4:100). The first and third yellow fractions were impurities and the second fraction was the product as a white solid. Yield: 65.0 mg, 14 %

HRMS (ESI)
[M+Na]^+ 1298.4362 m/z (measured), 1298.4369 m/z (calculated): C_{75}H_{65}N_{15}O_{15}Na

^1H NMR (500 MHz, CDCl₃): δ = 10.93 (s, 5 H, H10), 8.72 (d, 5 H, J = 3.2 Hz, H5), 7.59 (d, 5 H, J = 3.2 Hz, H3), 7.51 (d, 10 H, J = 7.4 Hz, H11), 7.43 (t, 10 H, J = 7.7 Hz, H12), 7.36 (d, 5 H, J = 7.2 Hz, H13), 5.20 (s, 30 H, H8), 4.01 (s, 15 H, H7)

^13C NMR (125 MHz, CDCl₃): δ = 162.22 (C9), 156.54 (C4), 140.81 (C1), 136.61 (C10), 133.70 (C2 or 6), 128.78 (C12), 128.25 (C13), 127.70 (C11), 126.02 (C2 or 6), 111.60 (C5), 111.09 (C3), 70.62 (C8), 63.57 (C7)

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Boron tribromide (0.008 mL, 0.078 mmol) was added to a solution of pentabenzyloxypentamer, **SP-4** (10 mg, 0.008 mmol) in dry DCM (20.0 mL) at 0 ºC. The mixture was stirred at r.t. overnight under N₂ atmosphere. The solution was decanted off. The remaining solid was washed with water, the solvent removed under vacuum, re-dissolved in MeOH and purified by preparative RP–HPLC (100% of water for 5 min and 0–100% of MeOH for 25 min) to give a white solid. Yield: approx. 1 µg

**HRMS (ESI)**

\[ [\text{M+Na}]^+ 848.2013 \text{ m/z (measured)}, 848.2022 \text{ m/z (calculated)}: \text{C}_{40}\text{H}_{35}\text{N}_{5}\text{O}_{15}\text{Na} \]
General Method F.

3-amino-2-fluorobenzoic acid, S-23 (0.167 g, 1.08 mmol) and MeCN (10.0 mL). Purification: After removal of the solvent, the residue was washed with MeOH (50.0 mL), DMF (20.0 mL) and DCM (50.0 mL x 2) to give an off-white solid. Yield: 7.00 mg, 4 %

HRMS (ESI)

$[\text{M+Na}]^+$ 708.1303 m/z (measured), 708.1277 m/z (calculated): $\text{C}_{35}\text{H}_{20}\text{F}_5\text{N}_5\text{O}_5\text{Na}$

$^1\text{H}$ NMR (400 MHz, DMSO): $\delta = 10.21$ (s, 5 H, $\text{Ha}$), 8.40 (td, 5 H, $^4J = 1.5$ Hz, $\text{H5}$), 7.65 (td, 5 H, $^3J = 1.7$ Hz, $\text{H3}$), 7.44 (t, 5 H, $^3J = 7.8$ Hz, $\text{H4}$)

The collected characterisations in this thesis corresponds to the literature values.\textsuperscript{114}
Cucurbituril

Cucurbit[5,6]uril, CB[5,6]\textsuperscript{11}

Method 1.\textsuperscript{11}

Glycoluril (5.68 g, 40.0 mmol) was suspended in 9 M H\textsubscript{2}SO\textsubscript{4} (20.0 mL) in a flask (50 mL). The mixture was heated at 70°C in an oil bath to dissolve the suspension and became a yellow solution. Formaldehyde (7.00 mL, 37% in water, 91 mmol) was added to the yellow solution which was stirred for 24 h at 70 - 75°C to give off-white precipitate, followed by another heating overnight at 95-100°C. After cooling to r.t., the mixture was poured into water (200 mL). Acetone (1.00 L) was then added to the mixture to precipitate CB[5,6,7,..] and then stood for 15 min. The supernatant solution was decanted and the remaining solid was washed with water/acetone mixture (1:4, 200 mL water / 800 mL acetone) twice. After filtration, water/acetone mixture (1:1, 100 mL water / 100 mL acetone) was added to the solid and the mixture was stirred for 10 min, followed by filtration, washed with cold water (100 mL) and dried under vacuum to give CB[6] as a white solid (4.94 g). Acetone (800 mL) was added to the colourless filtrate and the mixture stood for 15 min to precipitate. After filtration, washing with acetone and drying under vacuum, a mixture of CB[5] and CB[7] (1:1.5 = CB[5] : CB[7], 2.32 g) was produced. The mixture was re-dissolved in water (75.0 mL) and MeOH (75.0 mL) was added to precipitate CB[7] as a white solid which was filtered and washed with MeOH (10.0 mL). Acetone (300 mL) was added to the filtrate to produce precipitate (CB[5], 0.772 g) which was filtered, washed with acetone and dried under vacuum. The crude product was purified by recrystallization using diluted H\textsubscript{2}SO\textsubscript{4} at 5°C for 24 – 48 h to yield colourless needles/blocks. Yield: 0.130 g, 2%

HRMS (ESI)

# Caesium carbonate was added for ionisation.

[M+Cs]\textsuperscript{+} 963.1509 m/z (measured), 963.15 m/z (calculated): C\textsubscript{30}H\textsubscript{30}N\textsubscript{20}O\textsubscript{10}Cs
[M-H+2Cs]⁺ 1095.0492 m/z (measured), 1095.06 m/z (calculated): C₃₀H₂₉N₂₀O₁₀Cs₂

¹H NMR (300 MHz, D₂O): δ = 5.77 (d, 10 H, ²J = 15.3 Hz, Ha), 5.62 (s, 10 H, Hc), 4.44 (d, 10 H, ²J = 15.3 Hz, Hb)

¹³C NMR (75 MHz, D₂O): δ = 156.28 (O=C), 69.00 (Hc-C), 49.93 (Ha,b-C)

¹H NMR spectra of CB[6] and CB[7] correspond to the literature. Dramatic peak-shifts in ¹H NMR spectra were observed when adding 1,4-diaminobutane as a guest molecule to the NMR samples of CB[6] and CB[7] whereas no peak-shift occurred in ¹H NMR spectrum of CB[5] in the presence of 1,4-diaminobutane. This is due to the cavity size where the cavities of CB[6] and CB[7] are sufficiently large to allow the guest molecule to occupy in whereas the cavity of CB[5] is too small for 1,4-diaminobutane. This method of differentiating CB[5] from CB[6,7] is attributed to strong affinity of CB series to amino groups.

HRMS (ESI)
CB[6]=[M+2Cs]²⁺ 631.0527 m/z (measured), 631.0527 m/z (calculated): C₃₆H₃₆N₂₄O₁₂Cs₂
CB[7]= [M+2Cs]²⁺ 714.0781 m/z (measured), 714.0772 m/z (calculated): C₄₂H₄₂N₂₈O₁₄Cs₂
[M+Cs]⁺ 1295.2361 m/z (measured), 1295.2490 m/z (calculated): C₄₂H₄₂N₂₈O₁₄Cs

Method 2.²¹⁵
A mixture of glycoluril (6.10 g, 43.0 mmol) and paraformaldehyde (2.59 g, 85.9 mmol) was dissolved in ice-cold 36% HCl (36.0 mL) with stirring. The solid was gradually dissolved and formed a clear gel which was allowed to stand at r.t. for 10 min. The reaction mixture was heated at 50 °C for 19 h with stirring and poured into MeOH (1.00 L) to give white precipitate which was filtered, washed with MeOH, water, MeOH and diethyl ether and dried under vacuum. Oligomer was produced (Yield: 8.00 g, 92%).²¹⁶ A mixture of the oligomer (5.00 g) and KCl (1.25 g) in 32% HCl (27.0 mL) was heated at 90~100 °C for 3 h. After removal of the solvent under vacuum, the residue was redissolved in water (12.5 mL) and then the reaction mixture was neutralised with KHCO₃ and reheated at 105 °C for 1 min then cooled to 5 °C to give a white solid (CB[5] and CB[8] mixture) which was collected by filtration. The filtrate was mostly CB[6]. The filtered white solid was redissolved in hot conc. HCl (5.00 mL) and 5% NH₄Cl (20.0 mL) was added. The reaction mixture was heated to boiling until all the solid was completed dissolved, cooled to 5 °C, filtered (the filtrate was mostly CB[8]), dried under vacuum and redissolved in water (10.0 mL). KOH was added until pH was raised to 9 to give a white solid which
was filtered, washed with ice-cold water and thoroughly dried under vacuum. The crude was CB[5] with K⁺ and Cl⁻. Yield: 1.03 g, 15%

¹H and ¹³C NMR spectra correspond to the values synthesised by Method 1.

HRMS (ESI)
[M+2K]²⁺ 454.0864 m/z (measured), 454.0858 m/z (calculated): C₃₀H₃₀N₂₀O₁₀K₂
[M+2K+Cl]⁺ 943.1391 m/z (measured), 943.1411 m/z (calculated): C₃₀H₃₀N₂₀O₁₀K₂Cl

Method 3.

Conc. H₂SO₄ (480 mL) was slowly poured into water (480 mL) in a 2 L beaker with stirring. After cooled to r.t., glycoluril (240 g) and formaldehyde (372 mL, 35% in water) were added to the mixture. The yellow/light brown solution was heated at 107 °C for 18 h. This water-evaporating process gave white crystals in dark brown solution. The mixture was cooled to r.t. and filtered through a sinter funnel. The filtered white crystal is crude CB[6] and the dark brown solution (~600 mL) contains CB homologues.

The white crystal was washed with conc. H₂SO₄ until yellow/light brown impurities were washed out. The product was then transferred to a 2 L beaker and water (1.00 L) was added. After mixing up using a glass stirring rod, the mixture was filtered and washed again with water until the last drop of filtrate was at least pH 5. The wet product was transferred into a beaker and dried in an oven to give a white powder which is CB[6] (~170 g). If the wet product is too dry, the corresponding oven-dried product will be a rocky chunk, not a fluffy powder.

The dark brown CB homologue solution (200 mL) was transferred into a 2 L beaker. Water (400 mL) and acetone (1.20 L) were added with stirring. The brown creamy solution mixture was left overnight at r.t. The solution phase that contained CB[5] was collected by gravity filtration using filter paper. Another standing at r.t. for 24 h gave colourless crystals. If precipitate or white crystals form, the whole batch cannot be used. The supernatant was decanted into a 2 L flask. The crystal was collected by filtration through a sinter funnel, washed only twice with water/acetone mixture (1:2 = water : acetone) and dried under vacuum to give white powders, CB[5] (~500 mg). Acetone was added to the collected transparent supernatant with stirring until the solution became slightly cloudy. Water was added until the solution had just become transparent again. The mixture was left at r.t. for 24 h or more to grow

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colourless crystals which were collected by filtration through a sinter funnel, washed with washed only twice with water/acetone mixture (1:2 = water : acetone) and dried under vacuum to give white powders, CB[5] (approx. 1.5 g).

Characterised data correspond to the values synthesised by Method 1 above.
A mixture of glycoluril (15.0 g, 106 mmol), formaldehyde (24.6 mL, 37% in water), conc. H₂SO₄ (14.3 mL) and water (100 mL) was heated at 110 °C for 7 h and the temp was raised up to 180 °C. The reaction mixture was cooled to r.t., poured into water (250 mL) and filtered. The filtered solid was redissolved in conc. HCl (250 mL) and water (1.00 L) was added. The white solid was collected by filtration, washed with water and oven-dried to give light brown crystals. Yield: 12.8 g, 73%

Characterised data correspond to one synthesised by Method 1 above.
PerhydroxyCB[6], CB[6]OH

Method 1.
A mixture of CB[6] (10.0 g, 10 mmol) and K$_2$S$_2$O$_8$ (45.0 g, 166 mmol) in water (700 mL) was sonicated for 3 min and then heated at 85 °C for 12 h. After cooling to r.t., the solution phase was collected by paper-filtration with no vacuum and no washing. A mixture of THF (1.00 L) and MeOH (50.0 mL) was added to the filtrate to give white precipitate which was mostly potassium sulfate salt. The solution phase was collected by vacuum filtration using a sinter funnel and concentrated to 35.0 mL. Acetone (200 mL) was added to the concentrated solution to give white precipitate (Crude product-1). After vacuum filtration using a sinter funnel, Crude product-1 was dried under vacuum and the collected filtrate (Filtrate-1) was concentrated to 10 mL. Acetone (100 mL) was added to Filtrate-1 (10.0 mL) to give white precipitate (Crude product-2) which was dried under vacuum. One of the crude products was selected by $^1$H NMR spectroscopy ($^1$H NMR spectrum of crude product-2 may contain additional peaks). The selected crude product was redissolved in a mixture of MeOH and conc. H$_2$SO$_4$ (ratio = 1 g of product : 100 mL of MeOH : 1 mL of conc. H$_2$SO$_4$). The mixture was sonicated and filtered out the remaining solid which was the salt contaminant. Diethyl ether was added to the collected filtrate (ratio = 100 mL of MeOH : 1 mL of conc. H$_2$SO$_4$ : 200 mL of diethyl ether) to give the pure product which was filtered using a sinter funnel, washed with diethyl ether (50.0 mL) and dried under vacuum. Yield: 0.726 g, 2%

Elemental Analysis for (C$_{36}$H$_{36}$N$_{24}$O$_{24}$)(K$_2$SO$_4$)$_8$(H$_2$O)$_{13}$(H$_2$SO$_4$)$_3$: C-13.84, H-2.17, N-10.47, S-11.43 (found), C-13.90, H-2.20, N-10.80, S-11.34 (calculated)

$^1$H NMR (400 MHz, DMSO): $\delta$ = 7.87 (s, 12 H, $\text{OH}$), 5.36 (d, 12 H, $^2J = 15.0$ Hz, $\text{CH}$), 4.46 (d, 12 H, $^2J = 15.0$ Hz, $\text{CH}$)
HRMS (ESI)
[M+2K]^{2+} 633.0806 m/z (measured), 633.0799 m/z (calculated): C_{36}H_{36}N_{24}O_{24}K_{2}
[M+Na+K]^{2+} 625.0894 m/z (measured), 625.0929 m/z (calculated): C_{36}H_{36}N_{24}O_{24}NaK
[M+2Na]^{2+} 617.1030 m/z (measured), 617.1059 m/z (calculated): C_{36}H_{36}N_{24}O_{24}Na_{2}
[M-2H]^{2-} 593.1115 m/z (measured), 593.1094 m/z (calculated): C_{36}H_{34}N_{24}O_{24}

Method 2.76
A mixture of CB[6] (10.0 g, 10 mmol) and K_{2}S_{2}O_{8} (45.0 g, 166 mmol) in water (700 mL) was sonicated for 3 min and then heated at 85 °C for 12 h. After cooling to r.t., the solution phase was collected by paper-filtration with no vacuum and no washing. The filtrate was neutralised by adding KOH aqueous solution (25.0 g in 100 mL) to give white precipitate. The mixture stood for 3 h and the supernatant was carefully decanted off. The precipitate was collected by centrifuge and dried under vacuum to give a white powder which were CB[6](O\textsuperscript{+}K\textsuperscript{-})\textsubscript{12} with a lot of potassium sulfate salt.

The crude product was redissolved in a mixture of MeOH and conc. H\textsubscript{2}SO\textsubscript{4} (ratio = 1 g of product : 100 mL of MeOH : 1 mL of conc. H\textsubscript{2}SO\textsubscript{4}). The mixture was sonicated for 10 min (until the white powder became colourless) and the solution phase was collected by gravity filtration. Diethyl ether was added to the collected filtrate (ratio = 100 mL of MeOH : 1 mL of conc. H\textsubscript{2}SO\textsubscript{4} : 200 mL of diethyl ether) to give the pure product which was filtered using a sinter funnel, washed with diethyl ether (50.0 mL) and dried under vacuum. Yield: 2.01 g, 10%

CB[6](OH)\textsubscript{12}(K\textsubscript{2}SO\textsubscript{4})\textsubscript{2}(H\textsubscript{2}O)\textsubscript{8}(H\textsubscript{2}SO\textsubscript{4})\textsubscript{3} was obtained.

\textsuperscript{1}H NMR (500 MHz, DMSO): δ = 7.19 (s, 12 H, OH), 5.35 (d, 12 H, \textsuperscript{2}J = 15.1 Hz, CH), 4.45 (d, 12 H, \textsuperscript{2}J = 15.1 Hz, CH)

This preparation was developed by Dr. Narayanan Selvapalam at Pohang University of Science and Technology.
DecahydroxyCB[5], CB[5]OH\textsuperscript{76}

A mixture of CB[5] (10.0 g, 12.0 mmol) and K\textsubscript{2}S\textsubscript{2}O\textsubscript{8} (45.0 g, 166 mmol) in water (700 mL) was sonicated for 3 min and then heated at 85 °C for 12 h. After cooling to r.t., the solution phase was collected by paper-filtration with no vacuum and no washing. The filtrate was neutralised by adding KOH aqueous solution (25.0 g in 100 mL) to give white precipitate. The mixture stood for 3 h and the supernant was carefully decanted off. The precipitate was collected by centrifuge and dried under vacuum to give a white powder which were CB[5](O\textsuperscript{–}K\textsuperscript{+})\textsubscript{10} with a lot of potassium sulfate salt.

The crude product was redissolved in a mixture of MeOH and conc. H\textsubscript{2}SO\textsubscript{4} (ratio = 1.00 g of product : 100 mL of MeOH : 1.00 mL of conc. H\textsubscript{2}SO\textsubscript{4}). The mixture was sonicated for 10 min (until the white powder became colourless) and the solution phase was collected by gravity filtration. Diethyl ether was added to the collected filtrate (ratio = 100 mL of MeOH : 1 mL of conc. H\textsubscript{2}SO\textsubscript{4} : 200 mL of diethyl ether) to give the pure product which was filtered using a sinter funnel, washed with diethyl ether (50.0 mL) and dried under vacuum. Yield: 891 mg, 15%

\textsuperscript{1}H NMR (500 MHz, DMSO): \(\delta = 8.25\) (s, 10 H, \textit{OH}), 5.27 (d, 10 H, \(^{2}J = 14.2\) Hz, \textit{CH}), 4.44 (d, 10 H, \(^{2}J = 14.2\) Hz, \textit{CH})

This preparation was developed by Dr. Narayanan Selvapalam at Pohang University of Science and Technology.
Dimethylglycoluril, CB-1

A mixture of urea (150 g, 2.5 mol) and 2,3-butanedione (64.6 g, 0.75 mol) was stirred in water (750 mL) at r.t. Conc. HCl (20.0 mL) was added to the reaction mixture which was then stirred at r.t. for 3 days. White precipitate formed gradually. Filtration, washing with ice-cold water and EtOH and drying in an oven and under vacuum gave a light brown powder. Yield: 105 g, 80%

$^1$H NMR (500 MHz, DMSO): $\delta = 7.09$ (s, 4 H, NH), 1.31 (s, 6 H, CH$_3$)
Decamethyl CB[5], **CB[5]Me**

Water (3.36 mL) was added to dimethyl glycoluril, **CB-1** (2.69 g, 15.8 mmol) in conc. HCl (10.8 mL). Formaldehyde (5.68 mL, 68.9 mmol, 35% in water) was added to the reaction mixture which was then refluxed for 2 h. Water (47.0 mL) was added again and reflux was carried out for another 1 h. After cooled to r.t., white precipitate formed. Filtration, washing with ice-cold water twice and drying under vacuum gave a white powder. Yield: 0.385 g, 13%

$^1$H NMR (500 MHz, DMSO): $\delta = 5.67$ (d, 10 H, $^2J = 16.1$ Hz, $CH$), 4.46 (d, 10 H, $^2J = 16.1$ Hz, $CH$), 1.79 (s, 30 H, $CH_3$)

MALDI-TOF-MS

$[\text{M+H}]^+ 971 \text{ m/z (measured)}, 970.04 \text{ m/z (calculated): } C_{40}H_{51}N_{20}O_{10}$

CB[6]OH (0.311 g, 0.1 mmol) was added to a suspension of NaH (50% dispersion in mineral oil, 0.115 g, 2.4 mmol) in anhydrous DMSO (12.5 mL) at 0 °C and stirred at r.t. for 1 h. Allyl bromide (0.210 mL, 2.4 mmol) was added to the reaction mixture at 0 °C and stirred at r.t. for 12 h. The reaction mixture was poured into ice-water (100 mL) to give white/brown precipitate which was washed thoroughly with cold water and diethyl ether and dried under vacuum. Yield: 0.064 g, 38%

\textsuperscript{1}H NMR (400 MHz, DMSO): $\delta = 5.89$ (m, 12 H, $H5$), 5.66 (d, 12 H, $^{2}J = 15.2$ Hz, $H3$), 5.39 (dd, 12 H, $^{3}J = 14.7$ Hz, $H6$-cis), 5.21 (dd, 12 H, $^{3}J = 14.7$ Hz, $H6$-trans), 4.20 (d, 12 H, $^{2}J = 15.2$ Hz, $H3$), 4.04 (s_broad, 24 H, $H4$)

\textsuperscript{13}C NMR (100 MHz, DMSO): $\delta = 151.57$ (C1), 132.53 (C5), 117.60 (C6), 95.66 (C2), 64.88 (C4), 40.14 (C3)

HRMS (ESI) 
[M+2Cs]\textsuperscript{2+} 967.2023 m/z (measured), 967.2100 m/z (calculated): C\textsubscript{72}H\textsubscript{84}N\textsubscript{24}O\textsubscript{24}Cs\textsubscript{2}
Boronic acids

4-Bromo-2-butylbenzoic acid, B-1a

![Chemical Structure](image)

1-Bromobutane (0.740 mL, 6.85 mmol) was added to magnesium turnings (0.333 g, 13.7 mmol) in dry THF (7.00 mL) and the mixture was refluxed for 30 min. After cooled to r.t., the mixture was transferred to a solution of 4-bromo-2-fluorobenzoic acid (0.500 g, 2.28 mmol) in dry THF (5.00 mL) at 0 °C. The mixture was warmed to r.t. and stirred for 17 h under N2. Water (40.0 mL) was slowly added at 0 °C. The mixture was then acidified with 6 N HCl until pH 1-2 and extracted with EtOAc (30.0 mL x 2). The combined organic layers were washed with brine, dried over Na2SO4 and the solvent removed under vacuum to give a white solid. The crude product was purified by flash silica chromatography (eluent: CHCl3 to 30% of MeOH in CHCl3) to give a yellow solid. Yield: 0.396 g, 68%

HRMS (ESI)
[M-H]- 255.0026 m/z (measured), 255.0026 m/z (calculated): C11H12BrO2

1H NMR (500 MHz, CDCl3): δ = 7.74 (t, 1 H, J = 8.0 Hz, H2), 7.37 (ddd, 2 H, J = 1.6 Hz, H3,5), 2.94 (td, 2 H, J = 3.1 Hz, H8), 1.70, 1.69, 1.67, 1.66, 1.64 (p, 2 H, J = 7.1 Hz, H9), 1.41 – 1.32 (m, 2 H, H10), 0.94 (t, 3 H, J = 7.3 Hz, H11)

13C NMR (125 MHz, CDCl3): δ =197.88 (C7), 162.60 (C1 or 6), 160.55 (C1 or 6), 131.93, 131.90 (C2), 128.15, 128.12 (C3 or 5), 124.94, 124.83 (C4), 120.45, 120.24 (C3 or 5), 43.44, 43.39 (C8), 26.12 (C9), 22.44 (C10), 14.00 (C11)
4-Bromo-2-heptylbenzoic acid, B-2a (NEW)\textsuperscript{82}

![Chemical structure of 4-Bromo-2-heptylbenzoic acid]

1-Bromoheptane (10.8 mL, 68.5 mmol) was added to magnesium turnings (3.33 g, 137 mmol) in dry THF (50.0 mL) and the mixture was refluxed for 30 min. After cooled to r.t., the mixture was transferred to a solution of 4-bromo-2-fluorobenzoic acid (5.00 g, 22.8 mmol) in dry THF (50.0 mL) at 0 °C. The mixture was warmed to r.t. and stirred for 24 h under N\textsubscript{2}. Water (400 mL) was slowly added at 0 °C. The mixture was then acidified with 6 N HCl until pH 1-2 and extracted with EtOAc (200 mL x 2). The combined organic layers were washed with brine, dried over Na\textsubscript{2}SO\textsubscript{4} and the solvent removed under vacuum to give a white solid. The crude product was purified by flash silica chromatography (eluent: CHCl\textsubscript{3} to 30% of MeOH in CHCl\textsubscript{3}) to give a yellow solid. Yield: 1.82 g, 27%

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ = 11.59 (s, 1 H, \textit{H}\textsubscript{a}), 7.95 (t, 1 H, \textsuperscript{3}J = 7.9 Hz, \textit{H}2), 7.04 (ddd, 2 H, \textsuperscript{4}J = 2.0 Hz, \textit{H}3,5), 2.66 (t, 2 H, \textsuperscript{3}J = 8.0 Hz, \textit{H}8), 1.64 – 1.59 (m, 2 H, \textit{H}9), 1.36 – 1.24 (m, 6 H, \textit{H}10, \textit{H}11, \textit{H}12, \textit{H}13), 0.90 (t, 3 H, \textsuperscript{3}J = 7.0 Hz, \textit{H}14)

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ = 170.07 (C7), 162.72 (C1 or 4), 161.53 (C1 or 4), 152.42 (C6), 134.13 (C2), 124.29 (C3 or 5), 116.97 (C3 or 5), 35.90 (C8), 31.84 (C9), 31.64 (C10), 30.76 (C11), 29.17 (C12), 22.76 (C13), 14.16 (C14)
4-Bromo-2-(tert-butoxy)benzonitrile, **B-3a**

![Chemical Structure](image)

A solution of potassium *tert*-butoxide (2.81 g, 25 mmol) in dry THF (50.0 mL) was added to a solution of 4-bromo-2-fluorobenzoic acid (5.00 g, 22.8 mmol) in dry THF (50.0 mL) at -78 °C over 1 h. The reaction mixture was stirred for 30 min at -78 °C and slowly warmed up to r.t., followed by stirring at r.t. for 2 h. The mixture was then acidified with 2 M HCl until pH 4, extracted with diethyl ether, dried over Na₂SO₄ and the solvent removed under vacuum. The crude product was purified by flash silica chromatography (eluent: DCM : n-hexane = 1:1) to give a colourless oil. Yield: 4.48 g, 71%

**HRMS (ESI)**

[M+Na]⁺ 276.0001 m/z (measured), 275.9994 m/z (calculated): C₁₁H₁₂BrNona

**¹H NMR (400 MHz, CDCl₃):** δ = 7.42 (d, 1 H, ³J = 8.3 Hz, H2), 7.31 (d, 1 H, ⁴J = 1.7 Hz, H5), 7.20 (dd, 1 H, ⁴J = 1.7 Hz, H3), 1.49 (s, 15 H, H9)

**¹³C NMR (100 MHz, CDCl₃):** δ = 159.27 (C6), 134.28 (C2), 127.76 (C4), 126.31 (C3), 125.70 (C5), 116.74 (C7), 107.41 (C1), 83.48 (C8), 28.97 (C9)
4-Borono-2-butylbenzoic acid, B-1

2.5 M n-butyllithium in n-hexane (21.5 mL, 53.9 mmol) was added dropwise to a solution of 4-bromo-2-butylbenzoic acid (3.96 g, 15.4 mmol) in dry THF (200 mL) at -78 °C and the mixture was stirred at -78 °C for 10 min. Triisopropyl borate (12.5 mL, 53.9 mmol) was then added dropwise at -78 °C and the mixture was then stirred at -78 °C for 3 h. After warmed up to 0 °C, the reaction mixture was quenched with 2 N HCl (60.0 mL) and extracted with EtOAc (300 mL x 2). The combined organic layers were stirred with 2.5 N NaOH (160 mL) for 10 min. The collected aqueous layer was acidified to pH 3 with 6 N HCl, extracted with Ethyl acetate, dried over Na₂SO₄ and concentrated to give white precipitate which was washed with DCM, collected by filtration and the solvent removed under vacuum. Yield: 1.33 g, 39%

HRMS (ESI) 
[M-H]⁻ 220.1023 m/z (measured), 220.1027 m/z (calculated): C₁₁H₁₄BO₄

¹H NMR (500 MHz, MeOD): δ = 7.87 – 7.46 (m, 3 H, H₂, 3, 5), 2.97 (t, 2 H, ²J = 8.0 Hz, H₈), 1.60 – 1.54 (m, 2 H, H₉), 1.41 – 1.35 (m, 2 H, H₁₀), 0.95 (t, 3 H, ³J = 7.3 Hz, H₁₁)

¹³C NMR (125 MHz, MeOD): δ =171.81 (C₇), 144.02 (C₆), 137.43 (C₅), 133.07 (C₁), 131.98 (C₃), 130.39 (C₂), 125.46 (C₄), 35.39 (C₈), 35.07 (C₉), 23.81 (C₁₀), 14.28 (C₁₁)

¹¹B NMR (160 MHz, MeOD): δ = 18.54 (s, 1 B)
4-Borono-2-heptylbenzoic acid, **B-2 (NEW)**

2.5 M *n*-butyllithium in *n*-hexane (7.31 mL, 18.3 mmol) was added dropwise to a solution of 4-bromo-2-heptylbenzoic acid (1.82 g, 6.10 mmol) in dry THF (100 mL) at -78 °C and the mixture was stirred at -78 °C for 10 min. Triisopropyl borate (4.22 mL, 18.3 mmol) was then added dropwise at -78 °C and the mixture was then stirred at -78 °C for 3 h. After warmed up to 0 °C, the reaction mixture was quenched with 2 N HCl (25.0 mL) and extracted with EtOAc (30.0 mL x 2). The combined organic layers were stirred with 2.5 N NaOH (25.0 mL) for 10 min. The collected aqueous layer was acidified to pH 3 with 6 N HCl, extracted with Ethyl acetate, dried over Na$_2$SO$_4$ and concentrated to give white precipitate which was washed with DCM, collected by filtration and the solvent removed under vacuum. Yield: 0.413 g, 26%

**HRMS (ESI)**

[M-H]$^-$ 263.1466 m/z (measured), 263.1463 m/z (calculated): C$_{14}$H$_{20}$BO$_4$

$^1$H NMR (400 MHz, MeOD): δ = 7.76 – 7.46 (m, 3 H, H$_2$, 3, 5), 2.96 (t, 2 H, $^3$J = 7.9 Hz, H$_8$), 1.60 – 1.53 (m, 2 H, H$_9$), 1.35 – 1.29 (m, 8 H, H$_{10}$, 11, 12, 13), 0.91 (t, 3 H, $^3$J = 7.3 Hz, H$_{14}$)

$^{13}$C NMR (100 MHz, MeOD): δ = 162.72, 144.04, 137.09, 131.94, 131.56, 130.41, 35.34, 33.17, 33.01, 30.76, 30.26, 23.69, 14.41

$^{11}$B NMR (128 MHz, MeOD): δ = 18.76 (s, 1 B)
(3-(tert-butoxy)-4-cyanophenyl)Boronic acid, B-3 (NEW)\(^{82}\)

![Chemical structure image]

2.5 M \(n\)-butyllithium in \(n\)-hexane (21.2 mL, 52.9 mmol) was added dropwise to a solution of 4-bromo-2-(tert-butoxy)benzonitrile (4.48 g, 17.7 mmol) and triisopropyl borate (12.2 mL, 52.9 mmol) at -78 °C and the mixture was then stirred at -78 °C for 4 h. After warmed up to 0 °C, the reaction mixture was quenched with 2 N HCl (75.0 mL) and extracted with EtOAc (75.0 mL x 2). The combined organic layers were stirred with 2.5 N NaOH (75.0 mL) for 10 min. The collected aqueous layer was acidified to pH 3 with 6 N HCl, extracted with Ethyl acetate, dried over Na\(_2\)SO\(_4\) and concentrated to give white precipitate which was washed with DCM, collected by filtration and the solvent removed under vacuum. Yield: 1.11 g, 29%

HRMS (ESI)

\([\text{M-H}]^- 218.0993 \text{ m/z (measured), } 218.0996 \text{ m/z (calculated): } \text{C}_{11}\text{H}_{13}\text{BNO}_3\]

\(^1\)H NMR (500 MHz, MeOD): \(\delta = 7.58 – 7.50 \text{ (m, 3 H, } H_2, 3, 5)\), 1.45 (s, 15 H, \(H_9\))

\(^{13}\)C NMR (125 MHz, MeOD): \(\delta = 159.00, 142.12, 133.48, 131.05, 129.31, 128.77, 118.48, 82.99, 29.23\)

\(^{11}\)B NMR (160 MHz, MeOD): \(\delta = 18.54 \text{ (s, 1 B)}\)
References


## Appendix: Ellipsometry Data

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<tr>
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<th>Au (JC)</th>
<th>Au (JC H)</th>
<th>Au (MQ)</th>
<th>Au.mat</th>
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*Note: The table lists ellipsometry data for various conditions and materials, including gold (Au) and various depolarization phases.*
Thickness of gold / thickness of organic layer (Å), MSE (× 10⁻³). Bare is bare gold substrates before deposition. Depo-1 is after deposition without an organic layer model. Depo-2 is after deposition and polycarbonate (n = 1.560 and k = 0 at 530 nm) as a model layer. Depo-3 is after deposition and polystyrene (n = 1.600 and k = 0 at 530 nm) as a model layer. Au (JC), Au (JC_L H), Au (MQ) and Au.mat are referred to the literatures.¹¹⁸