Synthesis, Characterisation and Conformational Studies of Novel Functionalised Polyarene Dendrimers Containing Pentaaryl and Hexaaryl Branching Units

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Abstract

The University of Manchester
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Doctor of Philosophy in the Faculty of Engineering and Physical Sciences
Synthesis, Characterisation and Conformational Studies of Novel Functionalised Polyarene Dendrimers Containing Pentaaryl and Hexaaryl Branching Units
2015

Polyarene dendrimers are composed entirely of aromatic rings and are of interest as they possess rigid and shape-persistent structures, which have potential applications in materials chemistry and as scaffold for functional molecules. This thesis describes the synthesis and characterisation of a number of new polyarene dendrimers containing pentaphenylbenzene-like (pentaaryl dendrimers) and hexaphenylbenzene-like (hexaaryl dendrimers) branching units which are capable of focal and peripheral expansions.

These structures are based on terminal and internal 1,3-dialkyne cores, onto which two polyaryl sections were introduced via Diels-Alder reaction. These compounds possess inherent axial chirality as a result of the dialkyne position on the core, and a range of differently substituted polyaryl units which result in further chiral axes.

Several crystal structures of pentaryl dendrimers were obtained, with these crystallising either as meso conformers or conformers with $C_2$ symmetry. Introduction of a chiral auxiliary onto the central aromatic ring of these dendrimers provided evidence of the atropisomers in solution. These were studied via VT $^{13}$C NMR, revealing fast rotation and an energy barrier of about 66 kJ mol$^{-1}$. The presence of additional aromatic rings on a hexaaryl dendrimer enabled observation of atropisomerism in solution owing to the greater steric hindrance of rotation of its branching units about the chiral axes. Fluorine-containing analogues of these dendrimers were synthesised and subjected to conformational studies through $^{19}$F–$^{19}$F Exchange Spectroscopy (EXSY). Qualitative and quantitative analysis of the spectra revealed the kinetic and thermodynamic parameters, showing that the energy barrier of rotation of these dendrimers was within the range of 75-80 kJ mol$^{-1}$, which was sufficient for spectroscopic observation but not for physical separation.

Polyaryls with symmetry or lacking symmetry have been synthesised. The lack of symmetry was achieved by stepwise introduction of the polyaryl fragments. This demonstrates a route to polyaryls with sections possessing different structural features and thus potentially engineered properties and future chemical differentiations.
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No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university, or other institution of learning.

Ray Putra Prajnamitra
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Abbreviations

°C = degrees Celcius
ACN = Acetonitrile
AFM = Atomic Force Microscopy
APCI = Atmospheric Pressure Chemical Ionisation
ASAP = Atmospheric Solids Analysis Probe
BIRD = Bilinear Rotation Decoupling
BOR = Bestmann-Ohira Reagent
COSY = Correlation Spectroscopy
CLSA = Complete Lineshape Analysis
CPD = Cyclopentadienone
DCC = N,N-dicyclohexylcarbodiimide
DCM = Dichloromethane
DEPT = Distortion Enhancement by Polarisation Transfer
DFT = Density Functional Theory
DIPEA = N,N-diisopropylethylamine
DMAP = 4-Dimethylaminopyridine
DMF = N,N-dimethylformamide
DMSO = Dimethyl Sulphoxide
DNMR = Dynamic Nuclear Magnetic Resonance
ESI = Electrospray Ionisation
EXSY = Exchange Spectroscopy
FAB = Fast Atom Bombardment
FD = Field Desorption
FID = Free Induction Decay
FIDRES = Free Induction Decay Resolution
FTIR = Fourier Transform Infrared
GC-MS = Gas Chromatography-Mass Spectrometry
GNR = Graphene Nanoribbon
HBC = Hexa-peri-hexabenzocoronene
HMBC = Heteronuclear Multiple Bond Correlation
HMQC = Heteronuclear Multiple Quantum Correlation
HPLC = High Performance Liquid Chromatography
HRMS = High Resolution Mass Spectrometry
HSQC = Heteronuclear Single Quantum Correlation
Hz = Hertz
J = Joule
K = Kelvin
kJ = Kilojoule
LAH = Lithium Aluminium Hydride
MALDI-TOF = Matrix-Assisted Laser Desorption/Ionisation-Time of Flight
MEM = 2-Methoxyethoxymethyl
MF = Matched Filter
n-ESI = nano-Electrospray Ionisation
NMR = Nuclear Magnetic Resonance
NOESY = Nuclear Overhauser Effect Spectroscopy
OLED = Organic Light Emitting Diode
ORTEP = Oak Ridge Thermal Ellipsoid Plot
ppm = parts per million
PPTS = Pyridinium p-toluenesulphonate
PSYCHE = Pure Shift Yielded by Chirp Excitation
SEC = Size Exclusion Chromatography
S/N = Signal-to-noise
TBAF = Tetrabutylammonium Fluoride
TBAI = Tetrabutylammonium Iodide
TBDMS = t-Butyldimethylsilyl
TEM = Transmission Electron Microscopy
TFA = Trifluoroacetic Acid
THF = Tetrahydrofuran
TIPS = Triisopropylsilyl
TLC = Thin Layer Chromatography
TMS = Trimethylsilyl
TOCSY = Total Correlation Spectroscopy
VT = Variable Temperature
1 Introduction

1.1 History of Dendrimers

Dendrimers are a class of hyperbranched yet structurally perfect molecules which have a well-defined size as well as number of end groups.\textsuperscript{1-3} The word dendrimer is derived from the Greek \textit{dendron} (tree) and \textit{meros} (part) due to the resemblance of these molecules to a tree. Before the term ‘dendrimer’ was coined by Tomalia in 1985,\textsuperscript{3,4} this type of molecule was known as ‘cascade molecule’, which means that the molecule is synthesised through a stepwise process.\textsuperscript{1}

In general, a dendrimer consists of three distinct architectural regions where chemistry can occur; the core (focal moiety), the layers of branched repeat units and the periphery (surface) of the dendrimer (Figure 1-1).\textsuperscript{2,5} The core of a dendrimer exhibits a unique property that is different from its surroundings, owing to the special environment created by the branches. The layers of the branched repeat units will create a void that can shield a species trapped inside the dendrimer from the outside environment. The multivalent surface of the dendrimer determines its macroscopic properties.\textsuperscript{2}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{dendrimer_diagram.png}
\caption{Three main regions in a dendrimer.}
\end{figure}

Dendrimer research goes back as far as 1941 when Flory carried out a theoretical consideration of infinite polymer networks.\textsuperscript{3} In 1974, Vögtle and Weber synthesised many armed molecules (but not branched) and categorised them as ‘octopus molecules’.\textsuperscript{6} A few years later (1978), the group managed to synthesise the first dendrimer (compound 4) through a stepwise process (Scheme 1-1).\textsuperscript{7}
The synthesis of this molecule was carried out using two-fold Michael addition of an amine to acrylonitrile to produce dinitrile 1. The dinitrile was then subjected to a reduction process to obtain the amine groups in compound 2. Repetition of the Michael addition and reduction of the products afforded the first dendrimer molecule 4.

In 1981, Denkewalter and co-workers patented a pathway to synthesise polylysine dendrimers. Later in 1985, Newkome and co-workers managed to synthesise a water-soluble and highly branched compound with hydroxy groups (compound 11, Scheme 1-2) called the ‘arborol systems’ (from the Latin arbour that means tree).

In the same year, Tomalia and co-workers successfully synthesised and fully characterised a novel compound, which is now known as the poly(amidoamines) (PAMAM) dendrimer. Nowadays, PAMAM dendrimer is produced on kilogram scale and is already being commercially distributed. PAMAM dendrimer can be synthesised using an ammonia (12) core or ethylenediamine (14) core but the branching units are
usually made of both methyl acrylate (13) and ethylenediamine (14) units. Scheme 1-3 shows an example of several generations of PAMAM dendrimer bearing ammonia core along with their synthesis starting from the core.

Scheme 1-3 Several generations of PAMAM dendrimer. The dendrimer was synthesised from ammonia (12) as core, methyl acrylate (13) and ethylenediamine (14) as branching units to form the first generation PAMAM dendrimer (15). This was further reacted with the branching units to form the second generation (16) and third generation (17) of the dendrimer. Alkylation of the amino moiety with methyl acrylate (13) goes via Michael addition with 1,4-regioselectivity. Amidation with ethylenediamine (14) then goes via the reaction with methyl ester, therefore forming the next generation dendrimer. These reactions are repeated until the desired generation of PAMAM dendrimer is obtained.

Syntheses of the first dendrimer (4) and PAMAM dendrimers (15, 16, 17) were carried out through the method currently known as the divergent approach. In 1990, Hawker and Fréchet introduced the convergent approach of dendrimer synthesis. Since then, the development of dendrimer chemistry has grown rapidly.
1.2 Methods for Dendrimer Synthesis

There are two main methods which are commonly applied in the synthesis of dendrimers: the divergent approach and convergent approach. Several other recent synthetic methods are the orthogonal synthesis, double-stage convergent method, double-exponential method\(^3\) and click chemistry.\(^3,11\)

1.2.1 Divergent Approach

The divergent approach was first introduced by Vögtle and co-workers in 1978 as ‘cascade’ and ‘nonskid-chain-like’ method.\(^7\) In this method, the synthesis of dendrimer is initialised from its core. Layer by layer, new groups are attached repeatedly to the core until the intended degree of branching (generation) is obtained.

In order to obtain the first-generation of the dendrimer, a branched unit is attached to the core. The functional groups at the surface of the unit are then reacted with another building block. Activation of the building block will generate the next generation dendrimer (Scheme 1-4). Activation can be in the form of removal of a protecting group or other reactions such as those that were previously shown in the first step during the synthesis of compound 4. In some cases, such as during the synthesis of PAMAM dendrimer, activation is not needed.

![Scheme 1-4 Dendrimer growth by means of the divergent approach. The core is activated (purple to blue) and coupled with periphery moiety (yellow) repeatedly until the dendrimer with the desired generation is obtained.\(^3,5\)](image)

This approach is conceptually straightforward,\(^2\) but there are several drawbacks in
practice. During the synthesis step, the size of the dendrimer molecule increases, so the number of surface functionalities also increases. Therefore, in order to achieve higher generations of the dendrimer, the number of reactions that need to be performed on the molecule increases exponentially.\(^2,5\) This results in the exponential increase of incomplete reactions, thus the formation of structurally-flawed by-products.\(^5\) Due to their structural similarities, separation of the intended product from the by-products is difficult.\(^2,5\) To drive the reaction to completion, a large excess of reagent is needed (15-250 equiv. of ethylenediamine is usually used during the synthesis of PAMAM dendrimers)\(^3,4\) which can cause some difficulties during the purification of the product.\(^5\)

### 1.2.2 Convergent Approach

In 1990, Hawker and Fréchet introduced the convergent approach as a new method in dendrimer synthesis.\(^10\) In contrast to the divergent approach, the synthesis of dendrimers in this method is initialised from the periphery. From the periphery, work is carried out towards the core.

![Scheme 1-5 Dendrimer growth by means of convergent approach. The periphery is activated (orange to yellow) and coupled with monomer branching units (blue) repeatedly until the dendrimer with the desired generation is obtained. Once it is obtained, the growth is stopped by attaching the core, as shown in the last step.\(^2,5\)](image)

In this method, the periphery is activated and coupled to a multifunctional core unit called a monomer to afford the first-generation dendrimer.\(^5\) The focal moiety of the monomer is protected to prevent the dendrimer from reacting in a divergent way during the next reactions. Activation of the focal point and coupling with the monomer results in the higher generation dendrimer. To obtain even higher generation dendrimers, the
process is repeated again and ended with coupling to the core (Scheme 1-5).

The convergent approach has several advantages over the divergent approach. Contrary to the divergent approach, there is only a small amount of reactive group (yellow and blue) involved in the convergent approach. Therefore, there is no need to use a large amount of excess reagent in each step. Even if the reaction is incomplete, the mass difference between the intended product and the by-products is usually large enough for a straightforward separation. This is unlike the difficulty encountered for separation of by-products in the divergent approach. Since the synthesis of the dendrimer is carried out ‘backwards’, the likelihood of the occurrence of structural defects is low.\textsuperscript{2,5}

One drawback of this approach is that as the size of the dendrimer becomes larger, its focal point becomes more and more shielded by the dendrons. The steric crowding due to this growth decreases the reactivity of the focal point and makes the reaction slower and less efficient.\textsuperscript{2} This drawback means the convergent approach is used mainly for the synthesis of lower generation dendrimers.\textsuperscript{3}

1.2.3 Orthogonal Synthesis

Orthogonal synthesis was introduced by Spindler and Fréchet in 1993.\textsuperscript{5,12} In this method, there are two different branching units which are inert towards each other and upon \textit{in situ} activation the units undergo a coupling reaction and produce the intended dendrimer. Nevertheless, this method is not widely adopted due to the very strict structural requirements of the building blocks.\textsuperscript{3} The reaction step of this method is illustrated in Scheme 1-6.

\begin{center}
\textbf{Scheme 1-6} Orthogonal synthesis steps. Species in brackets represent the \textit{in situ} activation products and their reactions with the branching units.\textsuperscript{3}
\end{center}
1.2.4 Double-stage Convergent Method

In this method, the divergent and convergent approaches are both combined. The core is initially synthesised through the divergent approach, whilst the periphery is synthesised through the convergent approach. Coupling between the core and the periphery affords a high generation dendrimer. This method can also produce a dendrimer which has different inner and outer branching units.\(^3\) The reaction step of this method is illustrated in Scheme 1-7.

![Scheme 1-7 Double-step convergent method.\(^3\)](image)

1.2.5 Double-exponential Method

In 1995, Moore and co-workers introduced the double-exponential method.\(^5\) In this method, synthesis of the dendrimer is carried out in two directions, towards the core and periphery\(^3\) as illustrated in Scheme 1-8 below.

![Scheme 1-8 Double-exponential method.\(^13\)](image)
A single starting material containing several protected reactive groups is activated in two different ways to result in two partially deprotected compounds. These compounds can react with each other to form the first-generation dendrimer. When the dendrimer is subjected to the same treatment, it affords two other half-deprotected compounds which can react with each other to form the second-generation dendrimer. Repetition of the process affords higher generations of the dendrimers.

1.2.6 ‘Click’ Chemistry

Since its introduction in 2001 by Sharpless and co-workers, ‘click’ chemistry has been employed in numerous quantitative reactions. A reaction can be classified as ‘click’ chemistry if it gives high yields, has no by-products or readily separable by-products, easy product isolation, straightforward reaction conditions and is stereospecific.

One of the most utilised reactions in dendrimer synthesis that can be classified as ‘click’ chemistry is the azide-alkyne cycloaddition reaction. In 2004, Wu and co-workers successfully synthsised a dendrimer containing triazole rings by means of 1,3-dipolar cycloaddition using alkyne and azide compounds as starting materials. Recently, Aida and co-workers have also utilised the formation of triazole rings in the syntheses of dendritic scaffolds that have been used as molecular glues. Other research groups have also used ‘click’ chemistry for dendrimer synthesis. The reaction between an alkyne and an azide in general is exemplified in Scheme 1-9.

\[ \text{Alkyne} + \text{Azide} \xrightarrow{\text{Cu(II)}} \text{Triazole} \]

Scheme 1-9 Dendrimer growth using ‘click’ chemistry of alkyne and azide mediated by copper catalyst.

1.3 Structural Flexibility of Dendrimers

There are two structural types of dendrimers: dendrimers with flexible structures and those with rigid structures. The flexibility of the dendrimers is determined by the branching units. Branching units that are made up of alkyl chains are more flexible than those made up of aromatic rings.
1.3.1 Structurally Flexible Dendrimers

An example of a structurally flexible dendrimer is the PAMAM dendrimer (compound 17 in Scheme 1-3). PAMAM dendrimer 17 is synthesised using ammonia as the core but there are also other types of PAMAM dendrimers that are synthesised using different core molecules such as ethylenediamine (14) and triethanolamine (18), shown as compounds 19 and 20 in Scheme 1-10.

![Scheme 1-10](image)

Scheme 1-10 Second-generation ethylenediamine core-PAMAM dendrimer (19) and triethanolamine core-PAMAM dendrimer (20).

Aside from PAMAM dendrimers, there are also other dendrimers with flexible structures, such as the one developed by Killops and co-workers (Figure 1-2, compound 21). An example of a less flexible dendrimer, made up by the combination of short alkyl chains and aromatic rings has been synthesised by Pappo and co-workers (Figure 1-2, compound 22).

Synthesis of these dendrimers has shown that the flexibility of the whole dendrimer can be tuned by using different branching units with varying flexibility.
1.3.2 Structurally Rigid Dendrimers

The structurally rigid dendrimers are made up entirely of aromatic rings and are known as polyphenylene dendrimers. These dendrimers are also known to be shape-persistent. The aromatic rings within the dendrimers can be in the form of phenyl, pyridyl, carbazole or any other substituted aromatic rings, depending on the type of precursor used during the synthesis. In the rules of nomenclature, the term ‘phenylene’ is restricted to a disubstituted benzene ring (C₆H₄). Hence, ‘polyphenylene’ is not a suitable term for this type of dendrimer. Furthermore, the aromatic rings that make up the dendrimers are not only restricted to phenyl rings, as stated above. For these reasons, ‘polyarene’ is a better name for this class of dendrimer.³

The first polyarene dendrimers were reported by Miller and Neenan and co-workers in 1990 and 1992.²⁷,²⁸ By utilising palladium-catalysed Suzuki coupling, they managed to synthesise dendrimers containing 4, 10, 22 and 46 benzene rings which are shown in Figure 1-3 as compounds 23, 24, 25 and 26, respectively.
Another way to obtain a polyarene dendrimer is through the Diels-Alder cycloaddition reaction, which is also included by Sharpless as a ‘click’ reaction. The Diels-Alder reaction is usually used to obtain a benzene ring from an alkyne and a cyclopentadienone derivative. The alkyne acts as the dienophile whilst the cyclopentadienone derivative acts as the diene. A bridged carbonyl compound is formed as intermediate, and upon heating, a decarbonylation process takes place producing an aromatic ring along with the release of carbon monoxide as by-product (Scheme 1-11).

In 1997, Müllen and co-workers synthesised the first polyarene dendrimers using the Diels-Alder cycloaddition reaction. The polyarene dendrimers were synthesised from several variations of cores and tetraarylcylopentadienone derivatives. Several of the first synthesised polyarene dendrimers are shown in Figure 1-4. Darker areas in dendrimer 31 are the overlapping phenyl rings.
In order for the Diels-Alder cycloaddition and decarbonylation reactions to proceed smoothly, high temperature was required. The synthesis of all the dendrimers above were carried out at temperatures higher than 150 °C.\textsuperscript{29–32} To achieve such high temperature, a high boiling point solvent must be used. Two solvents which are commonly used for this reaction are diphenyl ether and \textit{o}-xylene.\textsuperscript{31} Sometimes, a 1:1 mixture of diphenyl ether and \textit{o}-methylnaphthalene is also used.\textsuperscript{29}

Very recently, Itami and co-workers have managed to synthesise a series of analogues of cyclopentadienone that can bear four different aromatic rings through programmed synthesis.\textsuperscript{33} The group had previously achieved programmed synthesis of various heteroaromatics bearing different aromatic rings.\textsuperscript{33} Multiple palladium-catalysed couplings of 3-methoxythiophene (32) afforded the tetraarylthiophene compound. Since the cycloaddition reactions did not take place using the thiophene compounds, they were oxidised with \textit{meta}-chloroperxybenzoic acid (\textit{m}-CPBA) to obtain the sulfoxide group. These sulfoxide-containing compounds, also called thiophene S-oxides, were able to undergo the cycloaddition reactions with alkynes in a similar manner to the cyclopentadienones (Scheme 1-12), releasing sulphur monoxide gas as the by-product.
Although the thiophene S-oxide has yet to be applied in the synthesis of polyarene dendrimers, the group has demonstrated its potential application by synthesising various hexaphenylbenzene derivative compounds Figure 1-5. Hexaphenylbenzene itself is the structural motif of polyarene dendrimers.

Aside from the Diels-Alder reaction, another way to obtain a polyarene dendrimer is through the cyclotrimerisation process. This process involves three alkyne molecules, uses Co₂(CO)₈ as catalyst and forms a new benzene ring (Scheme 1-13).
Perhaps one of the most interesting aspects of polyarene dendrimers is their ability to undergo cyclodehydrogenation reactions facilitated by Lewis acids to produce graphene-type compounds. Several systems which are known to facilitate this reaction are CuCl₂, AlCl₃ and 1,1,2,2-tetrachloroethane;³⁰ Cu(OTf)₂, AlCl₃ and CS₂;³⁴-³⁶ and FeCl₃ in CH₃NO₂ and CH₂Cl₂.³⁷ This reaction proceeds in a step-wise process.³⁸ An example of the reaction is shown in Scheme 1-14.

![Scheme 1-14](image)

Scheme 1-14 Cyclodehydrogenation of dendrimer 39 to obtain graphene-type compound 40.³⁴

The presence of AlCl₃ in both of the Cu(II)-AlCl₃ systems can cause Friedel-Crafts dealkylation reactions, migration of the alkyl substituents (if the starting material contains alkyl groups) or chlorination of the product. This results in the Fe(III)-CH₃NO₂ system being a superior choice for the cyclodehydrogenation reaction.³⁴,³⁸

### 1.4 Characterisation of Polyarene Dendrimers

There are several methods which are routinely used to characterise polyarene dendrimers. Spectroscopic and spectrometric methods such as NMR spectroscopy and mass spectrometry are used to determine the purity and structural perfection. Other methods such as AFM, TEM or SEC are used to determine the size of the dendrimer whether directly or indirectly.³⁹ Single-crystal X-ray crystallography has also been applied in order to see the structure of the dendrimer.⁴⁰

Mass spectrometry methods such as chemical ionisation (CI), electrospray ionisation (ESI), fast atom bombardment (FAB), field desorption (FD) and matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) are commonly used for the analysis. Mass spectrometry will show the monodispersity of the synthesised dendrimers and also
detect any imperfect branching which might occur during cycloaddition.\textsuperscript{39} Monodispersity can be seen by a narrow molecular weight distribution, which means that the dendrimer consists of homogeneous size molecules.\textsuperscript{3} However, due to the mass limitation, CI and FAB method can only be used to characterise dendrimers with mass lower than 3000.\textsuperscript{10,41} Therefore, higher generation dendrimers with mass higher than that are usually characterised by using either ESI or MALDI-TOF methods.\textsuperscript{41}

Owing to the large amount of aromatic protons and carbons within a dendrimer, signals in \textsuperscript{1}H and \textsuperscript{13}C NMR spectra might overlap with each other. The chance of the overlapping increases as the dendrimer grows, thus in cases like this, NMR does not give enough structural information in order to determine the structure of the dendrimer. However, in some cases where a distinguishable characteristic signal of one part in the dendrimer can be recognised, identification of the other signals is possible as well.\textsuperscript{39}

On the other hand, X-ray crystallography can be applied to see the precise structure of a dendrimer by determining the arrangement of atoms within the dendrimer molecule as well as the packing of the molecule in its crystal form. However, during crystallisation, polyarene dendrimers generally precipitate as amorphous powders instead of crystals. This is caused by the large amount of conformational isomers which are energetically similar and thus results in the lack of long-range order in the condensed phase.\textsuperscript{40,41}

### 1.5 Variations of Polyarene Dendrimer

As shown in the previous examples, variations in the cores used to synthesise dendrimers can affect the overall geometry of the resulting dendrimers, regardless of whether they are flexible dendrimers (compounds 17, 19, 20, 21 and 22) or rigid polyaryl dendrimers (compounds 26, 27, 28, 29, 30 and 31). The applications of varying cores are reviewed in more detail in the next section of this chapter.

Variations in the periphery, however, can result in differences in the properties of the dendrimers. Hydrophobic dendrimers containing polar peripheral groups such as carboxylates or oligoethylene glycols can be water soluble.\textsuperscript{5,42} Similarly, hydrophilic dendrimers can also be soluble in non-polar solvents when decorated with long alkyl chain on their periphery.\textsuperscript{5} All of this behaviour is observed in both flexible and rigid dendrimers.
1.5.1 Variations in Periphery

Variations in the periphery of polyarene dendrimers are the result of the variations in cyclopentadienone (CPD) derivatives employed during the reaction and subsequently, the precursors of the CPD themselves. The CPD derivatives can be obtained by two different methods of synthesis. The first one is through a [3+2] cycloaddition reaction of cyclopropenones and alkynes. This reaction is facilitated by rhodium(I) complex \([\text{RhCl(CO)}_2]_2\), as illustrated in Scheme 1-15 (a). An alternative way to obtain a CPD derivative is through a Knoevenagel condensation of a 1,3-diarylpropanone and a 1,2-diaryl-1,2-diketone under basic conditions (Scheme 1-15 (b)). This method is regarded as the most useful synthesis of CPD derivatives.

![Scheme 1-15 Synthesis of CPD derivatives. (a) Through rhodium(I)-catalysed [3+2] cycloaddition reaction; (b) Through Knoevenagel condensation.](image)

Several CPD derivatives which have been synthesised through the Knoevenagel condensations are exemplified in Figure 1-6.

![Figure 1-6 Several examples of CPD derivatives.](image)

1.5.2 Variations in Core

To be able to undergo the Diels-Alder cycloaddition reaction, the cores of polyarene dendrimers must contain at least one alkyne group. Some cores may have more than one alkyne group and thus can undergo more than one cycloaddition reaction. Several examples of cores that have previously been synthesised are depicted in Figure 1-7.
Given that some cores may not be commercially available, a synthetic strategy is usually needed. The synthesis pathway for the cores may vary depending on the structure of the intended core. The most important step in the synthesis of cores however, is the introduction of alkyne groups because the presence of these groups is necessary for the subsequent cycloaddition reaction.

A common method for incorporation of an alkyne group into an aromatic compound is through the palladium-catalysed Sonogashira coupling.\textsuperscript{29,30} The synthesis of all the alkynes shown in Figure 1-3 involved the Sonogashira coupling. In the coupling process, an alkyne group was introduced to the aromatic ring in the form of a silyl ether-protected ethynyl group. Successive coupling of the alkyne and deprotection of the silyl ether protecting group afforded the intended core. Synthesis of compound 45 is used as an example for the process, as shown in Scheme 1-16.\textsuperscript{32}

Another way to introduce an alkyne group is by transforming an aldehyde using a phosphonate reagent known as the Bestmann-Ohira reagent (51) (Scheme 1-17). The reagent was discovered by Ohira\textsuperscript{45} and employed in the synthesis of alkynes by Bestmann.\textsuperscript{46}
Scheme 1-17 Synthesis of alkyne using Bestmann-Ohira reagent 51.46

Before compound 51 was reported, another type of phosphonate reagent was used for the conversion of aldehyde or aromatic ketones to alkyne.47 The reagent is known as the Seyferth-Gilbert reagent (Figure 1-8, compound 52).46,48–50 This reagent can react with bases such as n-BuLi or t-BuOK to produce an anion that reacts with the aldehyde or aromatic ketone to produce the alkyne, but it has to be freshly prepared and has to be isolated at -78 °C prior to its usage, which is its main drawback.46

Figure 1-8 Seyferth-Gilbert reagent (52) and the anion it produces (53).47

In 1989, Ohira discovered another type of phosphonate reagent which does not need to be isolated at -78 °C but can still form compound 52 upon methanolyis.45 In 1996, Bestmann and co-workers found that the reagent that Ohira discovered could also be used for the synthesis of alkynes by in situ generation of anion 53 through methanolyis under slightly basic conditions.46 Since then, the reagent has been known as the Bestmann-Ohira reagent (51).

Scheme 1-18 Synthetic pathway of core 48.32
A more complex synthetic pathway can be observed in the synthesis of hexaphenylbenzene core 48 (Scheme 1-18). Subsequent Sonogashira couplings, Diels-Alder cycloaddition and deprotection of the alkynes successfully furnished the core in a very good yield.32

1.6 Properties of Polyarene Dendrimers

Polyarene dendrimers are known to have high thermal stability due to the large number of aromatic rings within the structures.39 By means of thermogravimetric analysis, thermal stability of dendrimers 23, 24, 25 and 26 (Figure 1-3) was investigated by Miller and co-workers;28 while dendrimers 29 and 30 (depicted in Figure 1-4) were investigated by Müllen and co-workers.31 It was found that 23 and 24 decomposed at temperatures higher than 200 °C and 400 °C respectively,28 while higher-generation dendrimers 25, 26, 29 and 30, decomposed at temperatures higher than 550 °C.28,31

Besides their high thermal stability, dendrimers 29 and 30 also have remarkable chemical stability. No decomposition was observed after both of the dendrimers were boiled in concentrated hydrochloric acid or 30% potassium hydroxide solution for seven days.31 The dendrimers however, were capable of reacting with strong electrophiles such as sulfuric acid, although the structure of the product of this substitution was not reported, no changes were observed within the polyarene network, indicating an aromatic electrophilic substitution reaction.31

Very recently, work by Brutschy and co-workers has shown that polyarene dendrimers are able to include small molecules within the cavity in their structures.51 They reported the ability of the first to fifth generation polyarene dendrimers (30 and 58-61, Figure 1-9 (a)) to include several alkylated benzene derivatives with various sizes as guest molecules (62-72, Figure 1-9 (b)). Even though higher generation dendrimers have better capability to include larger guest molecules, the fifth generation dendrimer (61) was reported to have less capability, presumably because of its densely packed periphery that prevents the guest molecules from accessing the cavity.

The research shows that increasing the number of layers in a polyarene dendrimer does increase the size of the void created but the ability of the dendrimer to include guest molecules also depends on its peripheral crowdedness. This only becomes apparent in
higher generation dendrimers owing to the higher number of peripheral moieties they possess.

![Figure 1-9](image)

**Figure 1-9** (a) Polyarene dendrimers first to fifth generations used in the study; (b) Alkylated benzene derivatives used as guest molecules.

In general, polyarene dendrimers have poor solubility in polar solvents such as methanol. In fact, the purification of polyarene dendrimers is usually carried out through precipitation in methanol. A recent study by Stangenberg and co-workers has shown that by attaching polar substituents on the periphery of polyarene dendrimers, the solubility of the dendrimers in polar solvents can increase.

The authors used second and third generation dendrimers 30 and 59 and several other analogues, and decorated their periphery with polar (sulphonic acid or phenylsulphonic acid) and non-polar (propyl) groups. The general structure of the substituted peripheral moiety as well as its substituents, shown in Figure 1-10, demonstrates this trend.

![Figure 1-10](image)

**Figure 1-10** Some of the dendrimers used in solubility study.
The solubility of these dendrimers is summarised in Table 1-1. It is clear that in general the first generation dendrimers have better solubility compared to their second generation counterparts (73 and 76, 74 and 77, 75 and 78). Higher generation dendrimers are also observed to have less solubility in polar solvents owing to the increased number of aromatic rings and therefore increasing their hydrophobicity. Interestingly, the fully sulfonated dendrimers (75 and 78), have better solubility in both polar and less polar solvents compared to the partially sulfonated ones (74 and 77) possibly due to the additional benzene ring that increases the hydrophobicity but at the same time, the increase in sulfonic acid group increases the hydrophilicity. Lower generation dendrimer 75 has better solubility than the higher generation dendrimer 78 which is consistent with the reasoning in the previous paragraph. All of these reasons can explain the solubility data observed for dendrimer 79.

<table>
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<tr>
<th>Solvents</th>
<th>73</th>
<th>74</th>
<th>75</th>
<th>76</th>
<th>77</th>
<th>78</th>
<th>79</th>
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<tr>
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<td>9.0</td>
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<tr>
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<td>1.4</td>
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<td>7.3</td>
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<td>Benzene</td>
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<td>3.2</td>
<td>43.1</td>
<td>0.9</td>
<td>4.2</td>
<td>10.4</td>
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<tr>
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<td>9.9</td>
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<tr>
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<td>1.6</td>
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<td>1.0</td>
<td>1.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 1-1 Solubility of dendrimers 73-79 in various solvents.42

The research shows that by changing the peripheral group, the solubility of polyarene dendrimers can change. Therefore, by careful selection of peripheral moiety, it is possible to tune the solubility of the resulting polyarene dendrimers.

Another interesting property of polyarene dendrimers is the conformation of each of the aromatic rings in the dendrimer. Due to steric hindrance, the aryl rings are rotated about the flexible C–C bond so that adjacent aromatic rings will be almost perpendicular to each other. In 1977, Gust investigated the rotation of phenyl substituents in hexaphenylbenzene (80) and found that the angle about the C–C single bond is about
65°. Hence, hexaphenylbenzene 80 adopts a conformation known as a propeller conformation, as shown in Figure 1-11.\textsuperscript{52}

![Figure 1-11 Propeller conformation of hexaphenylbenzene 80.](image)

Taking advantage of this behaviour, Figueira-Duarte and co-workers have synthesised several pyrene-containing polyarene dendrimers exhibiting axial chirality (Figure 1-12).\textsuperscript{53} The group has also managed to prove the presence of the isomers of polypyrene dendrimers through analytical HPLC.

![Figure 1-12 First (81) and second generation (82) of polypyrene dendrimers.](image)

1.7 Applications of Dendrimers

Dendrimers and dendritic scaffolds in general have been applied in various fields such as biological chemistry, host/guest encapsulation, sensor materials, organic light emitting diodes (OLEDs) and polymeric materials.\textsuperscript{54} Some recent applications, particularly those involving polyarene dendrimers, are reviewed here.

One of the most interesting applications of flexible dendritic scaffolds is a range of,
usually water-soluble, ‘molecular glue’ structures, developed by Aida and co-workers (Figure 1-13). They possess guanidinium ion moieties at the periphery which act as the adhesive, whilst various fluorescent compounds are used as the core.

The guanidinium ion pendant acts as an adhesive by forming a salt-bridge via electrostatic and hydrogen-bonding interaction between the guanidinium ions and the oxyanions that exist in proteins (Figure 1-14).

The group used compounds 83 and 84 to prevent microtubules from depolymerisation by tightly gluing their tubulin dimers together. They compared the activity of the
guanidinium pendants by using the linear version of the scaffold (rather than dendritic) and found that the dendritic scaffold gives better activity; this possibly stems from the conformational flexibility of the dendritic arms that makes it easier for the glue to adjust itself when anchoring onto the oxyanionic groups of the protein.\textsuperscript{55} They have also found that the higher generation dendrimer \textbf{84} exhibits better activity than the lower generation \textbf{83}, suggesting that multivalency plays an important role in the process.\textsuperscript{55}

The group have also used compounds \textbf{83} and \textbf{84} to successfully arrest the ATP-driven sliding motion of actomyosin, which is the motion responsible for muscle contraction.\textsuperscript{56} A modified version of compound \textbf{84} that bears benzophenone units next to the guanidinium pendants (compound \textbf{85}), was found to have better adhesion owing to the formation of covalent bond between the benzophenone unit to the protein surface after UV irradiation.\textsuperscript{17} This adhesion is then referred to as permanent fixation while the adhesion that makes use of only salt-bridges is referred to as temporal fixation. The adhesion strength of compound \textbf{85} before and after UV exposure was compared using optical tweezers\textsuperscript{17} and as expected, the permanent fixation shows stronger adhesion.

Another example of the application of molecular glue by Aida and co-workers is the third-generation dendritic compound \textbf{86} that was mixed with water, clay nanosheet and sodium polyacrylate to form mouldable hydrogels.\textsuperscript{57} The hydrogel is capable of self-healing when freshly cut and pushed together, forming material strong enough to be suspended horizontally (Figure 1-15 (a)) and vertically (Figure 1-15 (b)). The hydrogel can also be moulded to form a shape and it maintains the shape even after being immersed in THF for 6 hours three times (Figure 1-15 (c) and (d)). The authors noted that even after all the water in the hydrogel was replaced by THF, it still maintained its form and integrity, and that such organogel cannot be produced directly from THF.\textsuperscript{57}

![Figure 1-15](image-url) **Figure 1-15** Hydrogel made by mixing clay nanosheet, sodium polycrylate and compound \textbf{86}. (See main text for explanation, adapted from Wang \textit{et al.})\textsuperscript{57}

The hydrogel is capable of surviving moderately acidic or basic conditions (pH 4.0–10.0)
and salty water\textsuperscript{57} and can also incorporate biologically active proteins and transport them with maintained biological activity, albeit less than when the proteins are free. They demonstrated that myoglobin incorporated in the hydrogel is able to catalyse oxidation of \textit{o}-phenylenediamine with H\textsubscript{2}O\textsubscript{2}.\textsuperscript{57}

Polyarene dendrimers are also capable of incorporating guest molecules (Figure 1-9), and there are several other examples where guest molecules can be attached to, or incorporated within, the void of polyarene dendrimers through various mechanisms.\textsuperscript{58–60}

![Figure 1-16 Polyarene dendrimer structure used for covalent attachment study. (a) Main structure showing free thiol groups; (b) Attachment and controlled release of small molecule 88 to and from the dendrimer.\textsuperscript{58}](image)

Hammer and co-workers managed to perform covalent attachment of small molecules within the scaffold of a polyarene dendrimer followed by controlled release of the molecule under reductive conditions.\textsuperscript{58} The authors used 2-(4-nitrophenoxo)ethanethiol (88) as the guest molecule and attached it to the dendrimer scaffold (87) through formation of a disulfide bond. Quantitative cleavage of the disulfide bonds, yielding dendrimer 90, demonstrates the controlled release of the guest molecule (Figure 1-16).

The ability of the guest molecule to form the disulfide bond with the dendrimer is hampered by the size of the dendrimer cavity.\textsuperscript{58} The authors found that four guest molecules per host molecule was the upper limit, therefore they end-capped the free
thiol with methylbromide to prevent further disulfide bond formation. The MALDI-TOF mass spectra of dendrimer 89 before and after the end-capping process confirmed that there were four guest molecules attached as well as four residual thiols prior to end-capping. They also reported that the attached guest molecules are stable and capable of undergoing various purification steps.58

Another interesting host/guest interaction of polyarene dendrimers with guest molecules has been demonstrated by Nguyen and co-workers by using azo-benzene functionalities in the polyarene dendrimer scaffold.59 The azo-benzene moiety was able to undergo cis–trans isomerisation upon irradiation at 450 nm and 365 nm, consequently rendering the whole dendrimer structure ‘open’ and ‘closed’ upon irradiation (Figure 1-17).59

![Figure 1-17 Polyarene dendrimer containing azo-benzene moiety. (a) Main structure of the dendrimer (91) host showing azo-benzene moiety in red, drawn in 2D; (b) The ‘open’ and ‘closed’ 3D structures of the dendrimer triggered by irradiation at 450 and 365 nm, adapted from Nguyen et al.;59 (c) 4-Nitrophenol (92) used as the guest molecule.](image)

The ‘open’ structure of dendrimer 91 (trans) was loaded with the guest molecule 4-nitrophenol (92) and then closed with irradiation at 365 nm to form the cis isomer. The authors found that two guest molecules were sealed per host, and that the encapsulation of the molecule was proved to be stable even though the system was subjected to multiple purification techniques.59 They also found that release of the guest molecule could only be achieved when the encapsulated system was subjected to irradiation at 450 nm, transforming the dendrimer structure back to the ‘open’ state (trans isomer).59
Polyarene dendrimers have also been used for OLEDs owing to their highly conjugated systems. The dendrimers shown in Figure 1-18 have been shown to emit blue light. Other polyarene dendrimers decorated with several PMI chromophores (7-\(N\)-(2,6-diisopropylphenyl)perylene-3,4-dicarboximide), were reported to have fluorescent properties. An example of a first generation dendrimer fully decorated with PMI chromophores is compound 100 (Figure 1-19). A modified version of 100, in which one of the PMI substituents was changed to biotin (dendrimer 101), was used as a bioactive fluorescent probe.
Another piece of work by Sakamoto and Müllen in 2004 utilised the shape-persistent property of polyarene dendrimers to synthesise carbohydrate-containing dendrimers, also known as glycodendrimers. Shown in Figure 1-20 below, glycodendrimers 102 and 103 were reported to exhibit water-solubility. Interestingly the interior environment of dendrimer 103 maintained its hydrophobicity despite having sugar moieties inside it.\textsuperscript{65}

![Figure 1-20 Polyarene-based glycodendrimers 102 and 103.\textsuperscript{65}](image)

![Scheme 1-19 Synthesis of GNR 106.\textsuperscript{66}](image)

Narita and co-workers have synthesised graphene nanoribbons (GNRs) using a
polyarene dendrimer as a structural motif. An example of a GNR is compound 106, synthesised from CPD derivative 104, which undergoes Diels-Alder cycloaddition reaction with itself, followed by subsequent cyclodehydrogenation with the FeCl₃-CH₃NO₂ system. Although the strong aggregation nature of the GNR has made it difficult to obtain full characterisation, the authors proposed that the GNR may have promising application in nanoelectronics.

1.8 Design of New Polyarene Dendrimers

The most common method of growth of polyarene dendrimers has always been the Diels-Alder cycloaddition reaction of terminal alkynes with CPDs, therefore forming pentaphenylbenzene-like structures (Figure 1-10) as the branching units. Polyarene dendrimers, with multiple hexaphenylbenzene-like structures (Figure 1-11) as the branching units, grown with methods other than Diels-Alder, to the best of the author’s knowledge, have never been fully explored and there is only one reported example.

Most of the polyarene dendrimers to date were grown in an ‘all directions’ manner, in which all of the reactive parts of the core are reacted until they are fully exhausted. Consequently, the subsequent dendrimer growth can only be carried out through the reaction of the branching units with the one and only reactive moiety on the dendrimer: the peripheral moiety; this method is also known as the divergent approach. Some examples are dendrimers 28-31 that were synthesised from cores 45-48 respectively.

In comparison, there are several flexible dendrimers that were synthesised in a way where the growth is only performed on a part of the core, such as in dendrimers 4 and 83-85. This means that the dendrimer growth is not only limited to peripheral growth (divergent) but it is also capable of focal growth (convergent), and that the focal moiety can be grown in a completely different manner to the peripheral moiety.

There has only been one publication to date that addressed the synthesis of polyarene dendrimers through the convergent approach. The problem that the authors encountered was the steric hindrance of the dendrons that has affected the conformation of the focal moiety and made it difficult to obtain the next generation. They were only able to reach the second generation before the steric effects interfered. Consequently, they had to end the dendrimer growth early (first generation), add the core as the final
step and obtain second-generation dendrimers instead.\textsuperscript{31}

All polyarene dendrimers that have been reported to date have been symmetrical with each of the branches surrounding the core possessing the same repeating units and the same types of peripheral groups. The only dendrimers that possess different peripheral groups, such as dendrimers \textbf{89, 90} and \textbf{101}, were obtained by end-capping the periphery with different units. There are no reported polyarene dendrimers that are made unsymmetrical during the dendrimer growth.

In an endeavour to address all of the points above, this research envisages to synthesise new types polyarene dendrimers with various structural requirements and subsequently to study the resulting dendrimers and develop new expansion methods (other than Diels-Alder cycloaddition) as summarised below:

1. The resulting dendrimers have to possess hexaphenylbenzene-like structure branching units; those with pentaphenylbenzene-like structure units are also synthesised for comparison (Figure 1-21).

![Figure 1-21 Dendrimers with pentaphenylbenzene-like (left) and hexaphenylbenzene-like (right) branching units.](image)

2. The resulting dendrimers have to possess at least one unreacted functional group left on the focal moiety that is capable of focal growth (convergent). At the same time, the periphery must also contain reactive groups that are also capable of peripheral growth (divergent) (Figure 1-22).

![Figure 1-22 Dendrimer that is capable of focal and peripheral growth.](image)
3. Both of the focal and peripheral functionalities on the dendrimers should be capable of further dendrimer growth using methods other than Diels-Alder cycloaddition reaction. Furthermore, the growth of the periphery should not contribute too much to the crowdedness of the focal moiety so that the convergent growth can still be performed during the latter stages and vice versa.

4. The resulting dendrimers have to possess different peripheries (unsymmetrical) that are obtained during dendrimer growth (Figure 1-23); those that possess the same peripheries (symmetrical) are also synthesised for comparison.

![Figure 1-23](image-url) Unsymmetrical dendrimers as differentiated by the colours of the periphery.

5. Because these are new types of dendrimers, comparison of the properties between those containing pentaphenylbenzene-like and hexaphenylbenzene-like branching units as well as the comparison between the symmetrical and unsymmetrical dendrimers is a central aim.

To accommodate all of the requirements above, the author arrived at the general structures of dendrimers shown in Figure 1-24. The names of the categories (pentaaryl and hexaaryl) are derived from the types of structure that make up the branching units. The remaining unreacted group on the focal moiety that can be used as a site of future growth is shown as $R^1$. The $R^2$ and $R^3$ groups differentiate between symmetrical ($R^2 = R^3$) and unsymmetrical dendrimers ($R^2 \neq R^3$).

![Figure 1-24](image-url) General structures and classification of the target dendrimers.
It is obvious that pentaaryl and hexaaryl dendrimers possess different degrees of crowdedness due to the presence of an additional ring on the hexaaryl structure. It is also thought that the variations in the type of aromatic rings (hence variation in $R^4$) will affect the dendrimer structure, particularly the dendrimer conformation, and therefore the effects of using various $R^4$ groups are investigated. The study aims to investigate how to analyse the conformational differences between the pentaaryl and hexaaryl dendrimers, the symmetrical and unsymmetrical dendrimers as well as among hexaaryl dendrimers with different $R^4$ functional groups.

To achieve such structures, various building blocks and methods that are developed in this research are summarised below:

1. The core and periphery molecules should possess at least one different functional group, which is inert towards the Diels-Alder cycloaddition reaction, for subsequent focal growth.
2. The core and periphery molecules are designed so that the resulting branching units possess the desired type of units, either pentaphenylbenzene-like or hexaphenylbenzene-like units.
3. The core molecules for hexaaryl dendrimers are designed so that the effects of variations in $R^4$ functional groups on the conformation of the resulting dendrimers can be studied.
4. Development of new synthetic routes for polyarene dendrimers is needed to enable the synthesis of unsymmetrical dendrimers.
5. Both focal and peripheral functionalities should be capable of expansion with methods other than the Diels-Alder cycloaddition reaction.

It is hoped that this study will facilitate the development of new types of polyarene dendrimers, contribute to methods for structural study and thus assist in wider applications of dendrimers of these types.

Some of the direct advantages of the new dendrimers are predicted as follows:

1. The difference in crowdedness between pentaaryl and hexaaryl dendrimers can be used to tune the steric constraint of their higher generation versions by using combinations of both types of branching units (Figure 1-25).
Introduction

2. The focal moiety can enable growth of a polyarene dendrimer in a completely different manner than the peripheral growth. It is no longer restricted to Diels-Alder cycloaddition reactions but other reactions and also other building blocks. For example, the dendrimer can also be attached to other dendrimers (flexible or rigid) \textit{via} its focal moiety and therefore can be used to tune the size of cavity within the polyarene dendrimers (Figure 1-26) so it can perform better as a host.

3. Since the peripheral growth is in the direction away from the focal moiety, it only experiences little additional steric hindrance in the higher generation versions compared to the lower generations (Figure 1-27). This enables the convergent approach to be carried out even in higher-generation dendrimers.
4. In an unsymmetrical dendrimer, one part of the dendrimer can possess an entirely different property (e.g. polarity) from the other. This means that it can interact with various sites or molecules (e.g. protein) at once (Figure 1-28).

Figure 1-27 Polyarene dendrimer capable of both convergent and divergent growth.

Figure 1-28 Unsymmetrical dendrimer is capable of interaction with various sites with different properties.
2 Synthesis and Characterisations of Polyarene Dendrimers and Their Precursors

2.1 Retrosynthetic Analysis of Dendrimers and Their Precursors

As previously described in Chapter 1, the building blocks of polyarene dendrimers in this work are alkyne-bearing cores and cyclopentadienones (CPDs) which construct the peripheries, evident from retrosynthetic analysis (Scheme 2-1). In the case of symmetrical dendrimers, one-step Diels-Alder reactions between the core and periphery readily afford the target dendrimer. In unsymmetrical dendrimers, however, an intermediate compound, referred to as the monoadduct, needs to be prepared for subsequent reaction with a different periphery molecule.

![Scheme 2-1 Retrosynthetic analysis of dendrimers.](image1)

<table>
<thead>
<tr>
<th>Core</th>
<th>Dendrimer</th>
</tr>
</thead>
<tbody>
<tr>
<td>terminal dialkyne</td>
<td>monoalkyne</td>
</tr>
<tr>
<td>internal dialkyne</td>
<td>polyalkyne dendrimer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Core</th>
<th>Dendrimer</th>
</tr>
</thead>
<tbody>
<tr>
<td>terminal dialkyne</td>
<td>monoalkyne</td>
</tr>
<tr>
<td>internal dialkyne</td>
<td>polyalkyne dendrimer</td>
</tr>
</tbody>
</table>

![Scheme 2-2 Retrosynthetic analysis of terminal and internal dialkyne cores.](image2)
Most of the cores, particularly the internal dialkyne cores, are not commercially available and thus required synthesis. Retrosynthetic analysis of both terminal and internal dialkyne cores reveals their relationship to building blocks (Scheme 2-2). The choice of route for a given target dialkyne was determined by the availability of the starting materials.

The peripheries used in this project were introduced using CPD derivatives synthesised through the base-catalysed Knoevenagel condensation reaction. This was previously shown in Scheme 1-15 (b) in Chapter 1.

2.2 Synthesis of Cores

Ten different cores were used as building blocks for the dendrimers in this research. Each of these cores contains two alkyne moieties in meta positions relative to each other.

2.2.1 Synthesis of bis(Ethynyl) Compounds as Dendrimer Cores

Terminal bis(ethynyl) types of core were used to synthesise pentaaryl dendrimers (see Scheme 2-1, $R^4 = H$) since these program for a single C–H on the aromatic ring introduced via the Diels-Alder reaction. The terminal alkyne functionality was introduced using two methods: Seyferth-Gilbert homologation of dialdehyde groups, or Pd-catalysed Sonogashira coupling of haloaryl precursors with silyl-protected ethyne, followed by subsequent desilylation. The former involves a longer route but is significantly more cost-effective, whilst the latter involves a shorter route but is costly owing to the usage of a palladium catalyst. The bis(ethynyl) cores used in this research are shown in Figure 2-1.

![Figure 2-1 bis(Ethynyl) cores.](image)

Of these three, 1,3-diethynylbenzene (107) is the only one commercially available. The other two required synthesis. Core 108 was generated via Seyferth-Gilbert homologation, with a subsequent deprotection reaction providing core 109. An
alternative method to obtain core 109 was effected via Pd-catalysed Sonogashira coupling reaction. Both of these methods are appraised in the following section.

These three bis(ethynyl) cores, 107-109, were used not only to synthesise pentaaryl dendrimers but also as precursors to internal bis(arylethynyl) cores (Scheme 2-2). For this reason, large quantities of these cores were needed and hence efforts were directed towards optimisation aimed at high throughput and to ensure scalability.

2.2.1.1 Synthesis of bis(Ethynyl) Cores through Seyferth-Gilbert Homologation to Introduce Alkyne Moiety

The Seyferth-Gilbert homologation is a method to convert aldehydes and ketones into the corresponding alkynes by employing a phosphonate reagent to mediate the reaction. This method is potentially more cost-effective than the Sonogashira coupling reaction which employs Pd(0) as a catalyst. The syntheses of cores 108 and 109 were achieved through the synthesis outlined in Scheme 2-3.

![Scheme 2-3 Synthetic route of cores 108 and 109 using Seyferth-Gilbert homologation.](image)

The starting material in this route was 5-hydroxyisophthalic acid (110) which is commercially available. The first step was the esterification of carboxylic acid using methanol in acidic conditions. The product of this reaction was dimethyl 5-hydroxyisophthalate (111). Esterification took place in excellent yield (83%), improved further to 95% by employing anhydrous methanol.

The next step of the synthesis was the protection of the phenol group, which was important to prevent the phenol from interfering with later steps. The protecting group...
chosen was 2-methoxyethoxymethyl (MEM) group because of its stability towards mild acids, strong bases, organometallic reagents, reducing agents and oxidising agents.\(^{68}\)

The protection reaction was carried out using MEM-Cl (2-methoxyethoxymethyl chloride) under basic conditions (NaH) in tetrahydrofuran (THF) under N\(_2\) atmosphere,\(^{68,69}\) affording 112 in 69% yield. However, this was considered unsatisfactory because this compound was still far from the target compound and therefore a large amount was needed for the following steps. Moreover, a phenol protection might be anticipated to proceed with much higher efficiency. Though the THF used in the reaction had already been distilled over CaH\(_2\) prior to its usage, the presence of water in the THF was considered a possible cause for this outcome. Therefore, attempts to optimise yield were carried out by looking for ways to obtain drier THF.

Williams and Lawton reported that THF can be dried efficiently through storage over 3 Å molecular sieves (20% m/v) for 48-72 hours and that this treatment provide lower water ppm than traditional distillation alone.\(^{70}\) THF was therefore distilled over CaH\(_2\) and subsequently stored for at least 72 hours over 3 Å molecular sieves prior to its usage. These treatments managed to improve the yield of the reaction up to 96-98%.

The next step in the synthesis was the reduction of the ester groups of 112 to their corresponding alcohol which was effected using LiAlH\(_4\) in THF. The initial ester reduction procedure lead to 71% yield of diol 113, therefore, optimisation attempts were performed to obtain better yield.

Et\(_2\)O is a common solvent for LiAlH\(_4\) reduction, however, changing the solvent from THF to Et\(_2\)O evidenced poor solubility of 112 in Et\(_2\)O, and the reaction gave low yield (30%). Using THF that had been stored over 3 Å molecular sieves for 72 hours prior to usage led to an improved yield (80%), and when excess LiAlH\(_4\) was employed, a further increase in yield was obtained (85%).

The \(^1\)H and \(^{13}\)C NMR measurements as well as 2D HMBC experiment confirmed the structure of compound 113. The \(^1\)H and \(^{13}\)C NMR spectra also showed the presence of MEM, indicating that it had withstood the reduction reaction.

The initial proposal for synthesis of 108 was to convert both of the alcohol groups of
113 directly to terminal alkynes through a one-pot reaction. The oxidation of 113 to the corresponding aldehyde 114 was achieved using MnO₂, which would then undergo in situ alkynylation (Seyferth-Gilbert homologation) using the Bestmann-Ohira reagent (51) to afford 108.

The Bestmann-Ohira reagent was not commercially available at the time of this synthesis and had to be generated using a two-step procedure (Scheme 2-4). The synthesis of a diazo transfer reagent 115 in the first step was necessary since it would be employed in the diazo transfer reaction in the second step to obtain Bestmann-Ohira phosphonate reagent 51.

Two diazo transfer reagents that are commonly used are 4-toluenesulfonyl azide (tosyl azide) and 4-acetimidobenzenesulfonyl azide (115). The latter was chosen as the diazo transfer reagent in this reaction because it is considered safer than tosyl azide and is relatively cheap and easy to synthesise.

Compound 115 was prepared from 4-acetimidobenzenesulfonyl chloride (116), sodium azide and TBAI (tetrabutylammonium iodide (119)) as a phase transfer catalyst. The phase transfer catalyst facilitates the migration of the azide from aqueous phase to the organic phase via a mechanism illustrated in Scheme 2-5.

Once azide (120) has been transferred to the organic phase, it reacts with compound 116 through a nucleophilic substitution at the sulfone group to produce the diazo transfer reagent 115. The reaction afforded the azide in excellent yield (87%) with excellent purity.
Synthesis and Characterisations of Dendrimers and Their Precursors

Scheme 2-5 Reaction of TBAI (120) with sodium azide to facilitate azide transfer from aqueous phase to organic phase.

Though NMR spectra were consistent with those previously reported by Pietruzka and Witt,\textsuperscript{50} they were unreliable due to structural similarity between compound 115 and its starting material 116. Proof that compound 115 had been obtained was provided by infrared spectroscopy (Figure 2-2), which shows a strong band at 2117 cm\textsuperscript{-1} that corresponds to the stretching vibration of the azide functional group.

![Figure 2-2 FTIR spectrum of compound 115 (neat) showing strong azide vibration band.](image)

This diazo transfer reagent was then employed to obtain the Bestmann-Ohira reagent, dimethyl 1-diazo-2-oxopropylphosphonate (51). The diazo transfer mechanism is shown in Scheme 2-6.\textsuperscript{74}
The results of $^1$H and $^{13}$C NMR measurements were consistent with those previously reported by Pietruzka and Witt, including the heteronuclei $^1$H–$^{31}$P and $^{13}$C–$^{31}$P coupling constant values, which confirmed the successful formation of compound 51. Unfortunately, $^1$H and $^{13}$C NMR spectra suggested that this reagent trapped an amount of solvent used during purification (CH$_2$Cl$_2$), which caused difficulties in the following steps. Initial $^1$H NMR analysis showed 46 wt% of CH$_2$Cl$_2$ was present in the sample. Following extensive drying under high vacuum for two days, $^1$H NMR showed 44 wt% of CH$_2$Cl$_2$ was still present in the sample, showing that the treatment failed to effectively remove the remaining CH$_2$Cl$_2$. Nevertheless, it was later found that drying in smaller batches managed to remove most of the remaining solvent.

With Bestmann-Ohira reagent in hand, it was employed in the one-pot reaction to synthesise target core 108 (Scheme 2-7). The one-pot procedure is reported to produce alkyne compounds in high yield.  

Several attempts of this procedure failed to produce the intended dialkyne in good yield. The first attempt gave only 6% yield and whilst subsequent attempts afforded up to 40% yield, TLC and NMR analysis showed the presence of impurities which proved very difficult to separate. Overall, the reaction proved unpredictable and far too low-yielding to exploit.
Owing to these difficulties, the one-pot method was discontinued. A two-step reaction, involving oxidation of the alcohol 113 to aldehyde 114 and then a separate alkyynylation of aldehyde to form 108, was thus evaluated. This two-step synthesis greatly improved the yield and purity of the dialkyne product 108.

Oxidation of diol 113 to afford the aldehyde 114 was effected using MnO₂ as the oxidising agent. Though the MnO₂ oxidation is usually performed in CH₂Cl₂,⁷⁵ to mimic the conditions employed during the one-pot attempt, the reaction was initially attempted in THF. After 24 hours, only 16% yield of the partially-oxidised compound 121 (Scheme 2-8) alongside impurities were observed by NMR. Increasing reaction time to 48 hours in THF led to 40% yield of desired product 114, however impurities were still detected by NMR. These experiments suggest the oxidation takes place by oxidising one alcohol group at a time.

Oxidation of THF by MnO₂ to slowly form 1,4-butanedial has been reported.⁷⁶ The prior reaction times of 24 and 48 hours could favour this reaction and we thus concluded these solvent-related side-reactions most likely accounted for the poor performance of this reaction using THF. Hence, an alternate solvent (CH₂Cl₂) was considered. Change of solvent lead to improved yield (72%), shorter reaction time (24 hours) and more straightforward purification (Scheme 2-8).

Scheme 2-8 Summary of the oxidation attempts.

The final step in the synthesis of the core was the alkyynylation of the aldehyde through the Seyferth-Gilbert homologation reaction. The reagent 51 is effectively a pre-reagent, as the mechanism of the alkyynylation reaction is proposed to involve initial cleavage of the compound by methoxide generated from treatment of methanol with K₂CO₃ (Scheme 2-9 cf. Figure 1-8).⁷⁷ The cleavage of phosphonate 51 generates anion 53.
which is the active species that converts aldehyde into an alkyne group.\(^{45}\)

\[
\begin{align*}
(a) & \quad \text{CH}_3\text{OH} + \text{K}_2\text{CO}_3 & \rightleftharpoons & \quad \text{CH}_3\text{OK} + \text{K}_2\text{CO}_3 \\
(b) & \quad \text{114} + \text{53} & \rightarrow & \quad \text{122} + \text{108}
\end{align*}
\]

**Scheme 2-9** Formation of anion 53 from phosphonate 51. (a) Acid-base reaction between methanol and potassium carbonate;\(^{77}\) (b) Reaction with phosphonate 51 yields anion 53.\(^{45}\)

There are several mechanisms proposed for the conversion of aldehyde to alkyne. In a paper published in 1982, Gilbert and Weerasooriya explained in detail the role of anion 53 and solvent in the reaction (Scheme 2-10).\(^{47}\)

\[
\begin{align*}
\text{OMEM} & \quad \text{114} + \text{OMEM} & \rightarrow & \quad \text{OMEM} + \text{122} \\
\text{OMEM} & \quad \text{122} & \rightarrow & \quad \text{OMEM} + \text{108}
\end{align*}
\]

**Scheme 2-10** Reaction mechanism of the formation of dialkyne 108 from dialdehyde 114.\(^{47}\)

Initial synthesis led to the formation of monoalkyne by-product 122, due to the usage of reagent 51 that trapped an amount of CH\(_2\)Cl\(_2\). Monoalkyne 122 was readily converted to form dialkyne 108 (90% yield) using the same method but with an excess amount of Bestmann-Ohira reagent. The rest of the unreacted phosphonate reagent 51 was successfully recovered.

After the Bestmann-Ohira reagent was dried in smaller batches and most of the remaining CH\(_2\)Cl\(_2\) was removed, it was used once again in the synthesis of dialkyne 108. Using this cleaner reagent, 88% yield of dialkyne 108 was obtained and no monoalkyne 122 by-product was observed by TLC and NMR. Breaking the one-pot procedure for the synthesis of the dialkyne into two separate steps proves to greatly increase both the yield and purity of the product.
Core 108 was used as a precursor to synthesise additional cores and some dendrimers. Unfortunately, the deprotection of MEM in later stages proved to be difficult. It was decided that the core ought to be deprotected in an earlier stage to avoid future difficulties. MEM deprotection of core 108 afforded 3,5-diethynylphenol terminal alkyne core 109.

Deprotection of MEM is usually carried out using a Lewis acid as the deprotecting agent. Corey and co-workers reported that Lewis acids such as ZnBr$_2$ and TiCl$_4$ give the best yield. Other Lewis acids such as ZnCl$_2$, ZnI$_2$, SnCl$_2$, SnBr$_2$, ZrCl$_4$, MgCl$_2$ and MgBr$_2$ may also mediate the deprotection, but they are reported to have less efficiency.$^{68}$

Due to the hazardous nature of TiCl$_4$, ZnBr$_2$ was chosen as the deprotecting agent but the resulting reaction yielded 109 in a low yield (28%), hence, an alternative mild deprotecting agent was desired. Trifluoroacetic acid (TFA) has been reported to facilitate MEM deprotection at room temperature with short reaction time,$^{78}$ and when TFA was employed, 60% yield of 109 was obtained.

The overall yield of the synthesis of core 109 from compound 110 through the Seyferth-Gilbert homologation method was only 30%.

### 2.2.1.2 Synthesis of bis(Ethynyl) Core using Palladium-catalysed Sonogashira Coupling to Introduce Alkyne Moiety

One of the main drawbacks of using Seyferth-Gilbert homologation to introduce dialkyne moieties is the number of synthetic steps (6 steps), which consequently means that it takes a considerable amount of time to obtain the core, and has low overall yield (30%). Therefore, a shorter synthetic route by using a palladium-catalysed Sonogashira coupling method was evaluated (Scheme 2-11).

![Scheme 2-11](image)

Scheme 2-11 Synthetic route of core 109 using palladium-catalysed Sonogashira coupling.
3,5-Dibromophenol (123) was selected as the starting material. Protection of the phenolic alcohol was necessary but due to the difficulties experienced during the removal of MEM protecting group from core 109, a different protecting group, tert-butyl(dimethyl)silyl (TBDMS), was selected. This protecting group has been reported to possess stability at high temperature, making it a good choice to protect cores that will be subjected to Diels-Alder cycloaddition reactions. Furthermore, the removal of silyl protecting groups is relatively easy in comparison to MEM.

Protection of alcohols using TBDMS is typically performed by using imidazole as a base and a catalytic amount of DMAP. The reaction is thought to proceed via the formation of N-tert-butyl(dimethyl)silylimidazole, a very reactive silylating agent. Catalytic amount of DMAP assists in the deprotonation of the phenol so that it can become a better nucleophile. Using these reagents, protection of phenolic alcohol successfully produced 124 in 91% yield.

Introduction of dialkyne moieties to 124 was performed by Pd-catalysed Sonogashira coupling reaction using trimethylsilylacetylene as the alkyne source. In Pd-catalysed reactions, the palladium species used is usually in the form of active Pd(0) species such as Pd(PPh₃)₂, which is a 14-electron species. This species is usually generated in situ, due to its unpredictable nature and sensitivity to air. Several palladium sources which are commonly used as precatalysts are Pd(PPh₃)₄, Pd(PPh₃)₂Cl₂, Pd(dba)₂ (dba = trans-dibenzylideneacetone), Pd(OAc)₂ and PdCl₂. In this research, PdCl₂ and Pd(PPh₃)₂Cl₂ were used as precatalyst.

![Scheme 2-12](image)

(Scheme 2-12) Mechanism of reduction of Pd(II) to produce Pd(0).

Following treatment with triphenylphosphine, PdCl₂ generates Pd(PPh₃)₂Cl₂, which is then reduced by an amine to afford the active Pd(PPh₃)₂ species (Scheme 2-12).

The complex Pd(PPh₃)₂Cl₂ coordinates with the amine and subsequent β-hydride elimination followed by reductive elimination of hydrochloric acid produces Pd(PPh₃)₂.
The Pd(PPh$_3$)$_2$ generated then enters the catalytic cycle and catalyses the coupling reaction (Scheme 2-13).

Oxidative addition of the haloaromatic compound in (step i) produces the Pd(0) trans-complex. In a separate cycle, terminal alkyne metallates with Cu(I) halide to form copper(I) acetylide with the aid of the amine base. The alkyne from this complex then undergoes transmetallation with the Pd(0) complex as shown in (step ii), releasing Cu(I) halide. This new complex then undergoes subsequent cis-trans isomerisation (step iii) and reductive elimination (step iv) to give the coupling product and regenerate the active Pd(0) species. During the formation of a dialkyne product, the first coupling product (also called monocoupled product) re-enters the cycle to give the dialkyne product. This pathway led to the formation of compound 125 (90% yield) along with the formation of monocoupled by-product 126 (4% yield).

The final step is the deprotection of silyl protecting groups. This was performed by using tetrabutylammonium fluoride (TBAF), furnishing target core 109 in 97% yield. The spectroscopic data of core 109 obtained from this method were consistent with those obtained through MEM deprotection.

The overall yield of the synthesis of core 109 with this method was 79%. The Pd-catalysed Sonogashira coupling method was deemed superior to the Seyferth-Gilbert homologation method, requiring fewer steps and affording excellent yield.

### 2.2.2 Synthesis of bis(Arylethynyl) Cores as Dendrimer Cores

The bis(arylethynyl) core was used as a precursor to synthesise hexaaryl dendrimers.
The *bis*(arylethynyl) cores synthesised in this research are listed below (Table 2-1).

<table>
<thead>
<tr>
<th>Core</th>
<th>R</th>
<th>Ar</th>
<th>Core</th>
<th>R</th>
<th>Ar</th>
</tr>
</thead>
<tbody>
<tr>
<td>127</td>
<td>H</td>
<td>Ph</td>
<td>132</td>
<td>H</td>
<td>4-fluoro</td>
</tr>
<tr>
<td>128</td>
<td>OTBDMS</td>
<td>Ph</td>
<td>133</td>
<td>OH</td>
<td>4-fluoro</td>
</tr>
<tr>
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<td>H</td>
<td>2-pyridyl</td>
<td>134</td>
<td>H</td>
<td>2-fluoro</td>
</tr>
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<td>135</td>
<td>OH</td>
<td>2-fluoro</td>
</tr>
<tr>
<td>131</td>
<td>OH</td>
<td>2-pyridyl</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Table 2-1* *bis*(Arylethynyl) cores synthesised in this research.

### 2.2.2.1 Synthesis of Phenyl-containing Cores

Cores 127 and 128, although structurally very similar, were synthesised from different starting materials due to their availability (Scheme 2-14).

![Scheme 2-14](image)

Scheme 2-14 Synthesis of cores 127 and 128.

The reaction mechanisms of these syntheses follow the one previously established (Scheme 2-13). Due to the presence of copper as co-catalyst, homocoupled by-products were also observed. While structural assignments of both cores were confirmed using NMR methods, the structure of core 127 was further verified through X-ray crystallography (Figure 2-3).\(^1\)

The crystal of core 127 was obtained through slow evaporation of the solution in CH\(_2\)Cl\(_2\). It is interesting to see that in the crystal, all benzene rings in each core molecule exist on the same plane, making the molecule flat.

---

\(^1\) All X-ray crystallography characterisations of the cores and dendrimers in this thesis were performed by Moayad Khashoqji, Pritchard Group, The University of Manchester.
2.2.2.2 Synthesis of Pyridyl-containing Cores

In a procedure reported by Shi and Zhang in 2007, Sonogashira coupling took place under copper-free conditions using a mixture of acetone/water (1:1) as solvent. The palladium source used in this method was PdCl₂ and the base was piperidine.

Due to the formation of homocoupled by-products encountered during the synthesis of core 128, this copper-free method was assessed in the synthesis of pyridyl-containing cores 129-131 with the expectation that homocoupled by-products could be avoided. The three pyridyl-containing cores synthesised using this method are listed in Table 2-2.

![Diagram](a) (b) (c)

**Figure 2-3** X-ray crystallography of core 127. (a) Front; (b) Bottom; (c) Unit cell.

<table>
<thead>
<tr>
<th>Starting materials</th>
<th>R</th>
<th>Pyridyl cores</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>107</td>
<td>H</td>
<td>129⁺</td>
<td>49 (75)</td>
</tr>
<tr>
<td>108</td>
<td>OMEM</td>
<td>130</td>
<td>59</td>
</tr>
<tr>
<td>109</td>
<td>OH</td>
<td>131</td>
<td>52</td>
</tr>
</tbody>
</table>

⁺ The synthesis of this core was performed in conjunction with J. Mistry, Gardiner group.

Table 2-2 Synthesis of pyridyl containing cores 129, 130 and 131.

In 2003, Soheili and co-workers proposed a mechanism for the copper-free Sonogashira coupling reaction. The reaction that they carried out used (AllylPdCl)₂ complex as
palladium source and P(t-Bu)_3 as the phosphine ligand. \(^{83}\) In 2007, Tougerti and co-workers proposed a mechanism that was derived from the one proposed by Soheili. In their research, Tougerti and co-workers further refined the mechanism proposed by Soheili and proposed a detailed mechanism of the reaction (Scheme 2-15). \(^{84}\)

![Scheme 2-15](image)

**Scheme 2-15** Catalytic cycle of copper-free Pd-catalysed Sonogashira coupling reaction. \(^{84}\)

PdCl₂ is converted to give the active Pd(PPh₃)₂ in a manner that was previously described in Scheme 2-12. This Pd(0) species undergoes an oxidative addition reaction (step i). Complexation of the palladium complex with the alkyne, coupled by the loss of a triphenylphosphine ligand (step ii), yields the Pd-alkyne complex. Deprotonation of the acidic terminal alkyne proton by piperidine (step iii) is followed by reductive elimination which regenerates the active Pd(PPh₃)₂ catalyst and affords the monocoupled product.

Despite using a copper-free method to avoid the formation of homocoupling by-product, synthesis of these cores still gave moderate yields (about 50% on average). Core 129, also synthesised using the copper-assisted Sonogashira coupling method afforded the product in 75% yield, slightly better than the copper-free method. It is thought that the copper-free synthesis gave relatively moderate yields due to poor solubility of the starting materials owing to the presence of water. Another possible reason is that the reactivity of 2-bromopyridine (138) is less than that of 2-iodopyridine (139).

While NMR spectra confirmed the formation of all cores, X-ray crystallography further verified the structure of core 129 (Figure 2-4). The crystal of this core was grown from an acetone/water system through the vapour diffusion method. This core formed a
‘sandwich’ in its crystal packing and interestingly, the pyridyl ring orientations differ by layer. The first and third layers have a shared orientation but the second layer is different. Similar to core 127, the aromatics rings in each of the molecules are on the same plane, making the molecule flat.

Figure 2-4 X-ray crystallography result of core 129.

The first attempt to synthesise core 131 was performed through MEM deprotection of core 130, following a similar procedure to that used for the formation of 109, but the reaction generated unwanted by-products. The deprotection was first carried out using 10 equivalents of ZnBr₂. After overnight stirring in anhydrous CH₂Cl₂ at room temperature, a white precipitate formed in the reaction flask.

It was first assumed that this precipitate was the intended core 131, but further analysis (¹H NMR, solubility studies in various solvents and stoichiometry calculation of the precipitate) led to the conclusion that the deprotection reaction did not take place and the precipitate was most likely a complex between Zn(II) and core 130. The formation of the complex was favourable due to the presence of two pyridyl rings which could act as a bidentate ligand. Further characterisation of the precipitate was not pursued.

A second attempt to deprotect core 130 was carried out avoiding the use of Lewis acid to prevent formation of another complex. Monti and co-workers reported the use of 10
equivalents of pyridinium \( p \)-toluenesulphonate (PPTS) in either 2-butanol or \textit{tert}-butanol as an alternate method to deprotect MEM. Furthermore, they managed to deprotect several alcohols which could not be deprotected using Lewis acids. 

This deprotection strategy was attempted with both solvents. Unfortunately, the yields of both reactions were poor (13\% and 10\% in 2-butanol and \textit{tert}-butanol, respectively). This is likely caused by the formation of a salt between the pyridyl rings of core 130 with \( p \)-toluenesulfonic acid, which originated from PPTS.

Although there are other methods of MEM deprotection,\(^7\) consideration of the moderate yielding synthesis of core 130 (59\%) led to the discontinuation of attempts to synthesise 131 through this avenue. Instead, copper-free Sonogashira coupling of core 109 and 2-bromopyridine (138) generated core 131 successfully in a moderate yield (52\%) without further difficulties, despite having an unprotected phenol group in the starting material.

![Figure 2-5](image)

\textbf{Figure 2-5} X-ray crystallography result of core 131.

NMR spectroscopy and X-ray crystallography verified the formation of 131. The crystal of this core was grown from a hexane/acetone system through the slow evaporation...
As with core 129, the orientation of pyridyl rings in one core molecule is different. Intermolecular hydrogen bonds were observed between the hydroxy group of one molecule and the nitrogen in the pyridyl ring from another molecule. Interestingly, there was only one hydrogen bond formed between two core molecules (blue dashed line, Figure 2-5 (a)). The other pyridyl ring and hydroxy group formed intermolecular hydrogen bonds with other molecules (red dashed lines, Figure 2-5 (a)), and therefore the whole system formed a spiral network (Figure 2-5 (b)).

2.2.2.3 Synthesis of Fluorine-containing Cores
Following the decision to avoid copper-free Sonogashira coupling due to solubility issues, four fluorine-containing cores were synthesised through Pd-catalysed Sonogashira coupling (Table 2-3).

![Scheme 2-13](image)

<table>
<thead>
<tr>
<th>Alkyne starting materials</th>
<th>R</th>
<th>Iodobenzene starting materials</th>
<th>F</th>
<th>Fluorine-containing cores</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>107</td>
<td>H</td>
<td>140</td>
<td>4-Fluoro</td>
<td>132(^a)</td>
<td>81</td>
</tr>
<tr>
<td>109</td>
<td>OH</td>
<td>140</td>
<td>4-Fluoro</td>
<td>133</td>
<td>72</td>
</tr>
<tr>
<td>107</td>
<td>H</td>
<td>141</td>
<td>2-Fluoro</td>
<td>134(^a)</td>
<td>60</td>
</tr>
<tr>
<td>109</td>
<td>OH</td>
<td>141</td>
<td>2-Fluoro</td>
<td>135</td>
<td>59</td>
</tr>
</tbody>
</table>

\(^a\) The synthesis of these cores were performed in conjunction with J. Mistry, Gardiner group.

Table 2-3 Synthesis of fluorine-containing cores.

The synthesis follows the mechanism previously established (Scheme 2-13). There were no observed difficulties in the synthesis caused by the presence of unprotected phenol. The structures of the cores were confirmed by various NMR experiments. Since \(^{19}\)F nucleus is NMR active, the \(^{13}\)C peaks of carbons that were within four bonds of the fluorine split to form doublets due to coupling with \(^{19}\)F nuclei. Furthermore, \(^{19}\)F NMR experiments confirmed the presence of fluorine. These results showed a single fluorine peak for each core, indicating that all cores were symmetrical with both fluorines in each core being chemically equivalent.
2.3 Synthesis of Peripheries

Two CPD derivatives were used in this research, one that contained bromine (142) and the other fluorine (143) moieties. Their syntheses were carried out via Knoevenagel condensation of 1,3-diphenyl-2-propanone (144) with 4,4'-dibromobenzil (145) or 4,4'-difluorobenzil (146) respectively, under basic conditions (Table 2-4).86

In order to simplify the identification of peripheries, shorter names are assigned to these compounds by the author. Bromine-containing cyclopentadienone 142 (3,4-bis(4-bromophenyl)-2,5-diphenylcyclopenta-2,4-diene-1-one) is referred to as Br-CPD. Similarly, fluorine containing cyclopentadienone 143 (3,4-bis(4-fluorophenyl)-2,5-diphenylcyclopenta-2,4-diene-1-one) is referred to as F-CPD.

![Synthesis of cyclopentadienone (CPD) derivatives.](image)

<table>
<thead>
<tr>
<th>Benzil starting materials</th>
<th>X</th>
<th>CPDs</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>145</td>
<td>Br</td>
<td>142</td>
<td>83</td>
</tr>
<tr>
<td>146</td>
<td>F</td>
<td>143</td>
<td>83</td>
</tr>
</tbody>
</table>

Table 2-4 Synthesis of cyclopentadienone (CPD) derivatives.

Owing to the large number of aromatic protons within the compounds, several overlapping signals were observed in the \(^1\)H NMR spectra. Nevertheless, \(^1\)H and \(^13\)C NMR data of both compounds were consistent with those reported previously.44,86 The structure of each compound was further verified by X-ray crystallography (Figure 2-6).

![ORTEP drawing of Br-CPD (a) and F-CPD (b).](image)

**Figure 2-6** ORTEP drawing of Br-CPD (a) and F-CPD (b).
2.4 Rings and Axes Identification and Nomenclature of Dendrimers

As previously discussed, two types of dendrimers were pursued: pentaaryl (synthesised from \textit{bis}(ethynyl) cores) and hexaaryl (synthesised from \textit{bis}(arylethynyl) cores). The peripheries above were used in combination with both types of core to obtain a variety of pentaaryl and hexaaryl dendrimers with varying structures and characteristics.

In order to simplify the identification and discussion of the dendrimers and their aromatic rings in this thesis, the rings were labelled (Figure 2-7) and a naming convention for these dendrimers was developed by the author.

Due to the presence of rings G/G’ in the hexaaryl dendrimers, a slight difference in the naming system was required:

\textbf{For pentaaryl dendrimers:}

\begin{itemize}
  \item Class - Core Substituent - Left Periphery - Right Periphery
\end{itemize}

\textbf{For hexaaryl dendrimers:}

\begin{itemize}
  \item Class - Core Substituent - Aromatic Rings - Left Periphery - Right Periphery
\end{itemize}

In which,

\begin{itemize}
  \item \textbf{Class} refers to whether the dendrimer is ‘Penta’ (pentaaryl) or ‘Hexa’ (hexaaryl).
  \item \textbf{Core Substituent} refers to the substituent \(R^1\) on ring A in Figure 2-7. It is addressed as ‘H’, ‘OMEM’, ‘OTBDMS’, ‘OH’, etc.
  \item \textbf{Aromatic Rings} refers to rings G/G’, which are present only in the hexaaryl dendrimer class (Figure 2-7) and are addressed as ‘Phenyl’, ‘(2-Pyridyl)’, ‘(4-...
Fluorophenyl’ or ‘(2-Fluorophenyl)’. Parentheses are used for substituted aromatic rings.

- ‘Left Periphery’ and ‘Right Periphery’ refer to peripheral $R^2$ and $R^3$ substituents on rings D/E and D’/E’, respectively in Figure 2-7. They are addressed as ‘Br’ or ‘F’. This differentiation is important during the identification of unsymmetrical dendrimers. To further aid in discussion, bromine and everything on its side will be shown in purple whilst fluorine and everything on its side will be shown in orange.

Two of the dendrimers synthesised in this research can be used as examples. One of the pentaaryl dendrimers was named Penta-OH-Br-F and one of the hexaaryl dendrimers was named Hexa-OH-(2-Fluorophenyl)-Br-F.

In addition to the ring labelling and nomenclature, axes are an important part of the dendrimers. The main axes (blue in Figure 2-7) are referred to as the dendrimer arms and are present in both pentaaryl and hexaaryl dendrimers. Additional axes (red in Figure 2-7) are only present in the hexaaryl dendrimers and are referred to as the G/G’-rings axes. Both of them play an important role in contributing to the conformational descriptors of the dendrimers, and will be discussed in detail in Chapter 3.

### 2.5 General Synthesis and Characterisations of Dendrimers

![Scheme 2-16 Diels-Alder mechanism of alkyne cores and CPD to form the dendrimers.](image)

All of the polyarene dendrimers were synthesised through Diels-Alder cycloaddition between dialkyne cores and CPD derivatives at high temperature. The general
Synthesis and Characterisations of Dendrimers and Their Precursors

mechanism (Scheme 2-16) shows that the alkyne core reacts with the CPD, followed by extrusion of carbon monoxide (CO) to form the monoaduct. This then reacts with the remaining CPD (synthesis of symmetrical dendrimers) or is isolated and reacted with a different CPD (synthesis of unsymmetrical dendrimers) in a similar fashion to form the targeted dendrimer. The dendrimer is also referred to as the diadduct.

A drawback of this reaction is that CPDs degrade at high temperatures in the presence of oxygen by thermal oxidation. Thiemann and co-workers investigated this by heating several CPD derivatives (Table 2-5) in diphenylether at high temperature (135 °C) for 36 hours under air. They reported that two main products, ((Z)-diacylstilbenes and α-pyrones), as well as unreacted CPDs were obtained. The mechanism is not understood as the reactions were performed at high temperatures and thus the isolation of intermediates was difficult.

![Diagram](image)

<table>
<thead>
<tr>
<th>CPDs</th>
<th>-R'</th>
<th>Stilbenes (Yield)</th>
<th>α-Pyrones (Yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41</td>
<td>-Me</td>
<td>41-a (30%)</td>
<td>41-b (35%)</td>
</tr>
<tr>
<td>42</td>
<td>-OMe</td>
<td>42-a (22%)</td>
<td>42-b (17%)</td>
</tr>
<tr>
<td>142</td>
<td>-Br</td>
<td>142-a (26%)</td>
<td>142-b (20%)</td>
</tr>
<tr>
<td>143</td>
<td>-F</td>
<td>Not isolated</td>
<td>143-b (20%)</td>
</tr>
<tr>
<td>147</td>
<td>-H</td>
<td>147-a (27%)</td>
<td>147-b (24%)</td>
</tr>
<tr>
<td>148</td>
<td>-(4-OMe)Ph</td>
<td>148-a (25%)</td>
<td>148-b (17%)</td>
</tr>
<tr>
<td>149</td>
<td>-(4-OCF3)Ph</td>
<td>149-a (17%)</td>
<td>149-b (23%)</td>
</tr>
</tbody>
</table>

Table 2-5 Some of the CPDs and their thermal oxidation products.

To overcome this, the Diels-Alder reactions were always performed under nitrogen atmosphere. However, CPD degradation periodically occurred and made purification difficult. Purification of polyarene dendrimers is usually carried out by precipitation in polar solvents such as methanol, ethanol, acetone or acetonitrile. Unfortunately, most of the dendrimers synthesised in this research required purification via chromatographic separation, largely due to the solubility of the dendrimers in the aforementioned solvents. This was particularly evident with dendrimers possessing hydroxy groups on ring A. When separation of dendrimers from CPD degradation by-products could not be achieved by chromatographic separation alone, subsequent precipitation was also performed.
During the synthesis of symmetrical dendrimers, excess CPDs (3.0 equiv.) were employed to ensure complete reaction. The reaction took place as shown in Scheme 2-16, forming the targeted diadduct. In most reactions, the cores were fully consumed and only excess CPDs remained. Purification by flash column chromatography was therefore straightforward and the purity of the product was usually excellent.

Synthesis of unsymmetrical dendrimers required two sequential steps, where different peripheries were attached in each step. The monoadduct was the target compound in the first step, and excess core was used during the synthesis. Frequently, the synthesis could be visually tracked as the deep purple colour of the CPD disappeared, which was always in agreement with TLC analysis. The main problem faced during the synthesis was the formation of undesired symmetrical dendrimers as by-product, consequently lowering the yield of the monoadducts. Several optimisation attempts were carried out to suppress the formation of this by-product, such as decreasing the reaction temperature and varying the amount of excess core, however no considerable changes in the yield were observed.

Isolation of the monoadducts proved to be another challenge. Separation from the remaining core and symmetrical dendrimer by-product was initially attempted using flash column chromatography. However, it was very difficult because the polarity of the monoadduct was very similar to the by-product and the core. Frequently, these three species were inseparable. Furthermore, degradation of the CPDs sometimes took place during the reaction and the presence of the by-products made the purification more difficult. The most effective purification method was often either preparative TLC or reverse-phase HPLC.

Once the monoadduct was isolated, it was subjected to a second Diels-Alder cycloaddition using a different type of periphery to afford the unsymmetrical dendrimer. Excess periphery (up to 3.0 equiv.) was employed to ensure completion and decrease reaction time. The purification of unsymmetrical dendrimers was typically straightforward due to the absence of monoadducts.

Traces of solvents used during the purification usually remained in the samples and were always detected by NMR (sometimes even in the $^{13}$C NMR). The most common solvent trace was hexane but sometimes CH$_2$Cl$_2$, EtOAc, acetone and acetonitrile were
also observed. Leaving the samples under high vacuum for several days did not result in removal of these traces. Some samples that had been stored for about a year still showed the presence of hexane when the NMR measurements of these samples were rerun. It is likely that the conformation of these dendrimers has made it possible for the inclusion of these solvent molecules within the cavity and made it difficult for them to be removed. The ability of polyarene dendrimer to trap guest molecules has previously been shown in several examples in Chapter 1.  

Owing to the large number of aromatic protons within all of the dendrimers, there were a lot of peak overlaps in the $^1$H NMR spectra. The $^{13}$C NMR spectra were better resolved than the $^1$H NMR, however, due to the naturally low abundance of $^{13}$C isotope as well as the large number of carbon atoms within the dendrimers, a large amount of sample (about 50 mg) and a large number of scans were needed to obtain $^{13}$C NMR spectra with good signal-to-noise (S/N) ratio. In some hexaaryl dendrimers, however, it was not possible to obtain good $^{13}$C NMR spectra due to the presence of several conformers; this is explained in detail in the next sections and in Chapter 3.

Aside from the FT NMR spectroscopy characterisations, other physical properties and structural characterisation such as melting point, UV/Vis spectroscopy, fluorescence spectroscopy, FTIR, X-ray crystallography and mass spectrometry (MALDI) were also performed on these dendrimers. It was not possible to obtain accurate elemental analyses due to the presence of residual solvents in the samples. Müllen and co-workers also noted that the large number of carbon in the molecule could lead to incomplete combustion and therefore yielding inaccurate results. Due to these reasons, the elemental analyses were not performed.

Owing to the difficulties described above, mass spectrometry became the only reliable method to prove that the formation of products was successful. It was used not only to determine the mass of the dendrimers but also to confirm the isotope distributions pattern. Although providing no structural information, it was still able confirm in high certainty that the product was the targeted dendrimer, because the only structure that can be obtained from the Diels-Alder reaction that gave rise to such a mass is the intended structure. If there had been any by-product or structural defects formed during the course of the reaction, they would have yielded other peaks at much higher or lower $m/z$ than the intended dendrimer.
The synthesis described in this chapter is only of the main dendrimers. There are other
dendrimers that were derivatised from these dendrimers, synthesised to specifically be
applied for other purposes such as chiral resolution, conformational studies and
dendrimer expansion. The derivatisation and other studies of these dendrimers are
described in the later chapters.

2.6 Synthesis of Pentaaryl Dendrimers

Pentaaryl dendrimers were synthesised from combinations of bis(ethynyl) cores and
cyclopentadienone derivatives. This type of core has lower steric hindrance and
therefore, the Diels-Alder reactions progressed more quickly. The reactions were
usually complete in less than an hour, but were often left for several hours or overnight
to ensure completion.

Due to the complexity of overlapping peaks in the NMR spectra, unambiguous
assignment of quarternary $^{13}$C peaks could only be performed to a certain extent.
Definitive structural proof was obtained from X-ray crystallography for some of the
dendrimers. All of the pentaaryl dendrimers formed were subjected to crystallisation but
only two of the symmetrical dendrimers and one of the unsymmetrical dendrimers
formed crystals of sufficient quality for X-ray crystallography analysis. Vapour
diffusion method was found to afford the best dendrimer crystals (Figure 2-8, Figure 2-9
and Figure 2-14).

2.6.1 Synthesis of Symmetrical Pentaaryl Dendrimers

![Synthesis of Symmetrical Pentaaryl Dendrimers](image)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>Ring A</th>
<th>Rings D/E</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>H</td>
<td>Br</td>
<td>Penta-H-Br-Br</td>
<td>60</td>
</tr>
<tr>
<td>151</td>
<td>H</td>
<td>F</td>
<td>Penta-H-F-F</td>
<td>61</td>
</tr>
<tr>
<td>152</td>
<td>OMEM</td>
<td>Br</td>
<td>Penta-OMEM-Br-Br</td>
<td>77</td>
</tr>
<tr>
<td>153</td>
<td>OH</td>
<td>Br</td>
<td>Penta-OH-Br-Br</td>
<td>78</td>
</tr>
<tr>
<td>154</td>
<td>OH</td>
<td>F</td>
<td>Penta-OH-F-F</td>
<td>92</td>
</tr>
</tbody>
</table>

*a* These dendrimers were synthesised in conjunction with J. Mistry, Gardiner group.

*b* Obtained from Diels-Alder reaction instead of MEM deprotection.

Table 2-6 Synthesis of symmetrical pentaaryl dendrimers and their respective yields.
Five symmetrical pentaaryl dendrimers were synthesised in good to excellent yields as summarised in Table 2-6. Since these are symmetrical dendrimers, R² and R³ are the same and only shown as R².

Dendrimer 153 was initially synthesised through MEM-deprotection reaction of dendrimer 152, but it turned out that the deprotection was a difficult reaction and that the yield obtained was low. Since a large quantity of the hydroxy containing dendrimer 153 was needed as a building block for other derivatives, the MEM-deprotection route was not further pursued. The synthesis of dendrimer 153 was instead carried out via Diels-Alder cycloaddition reaction of core 109 with the Br-CPD periphery. For the same reason, MEM-containing dendrimers with peripheral fluorines were not synthesised; instead the OH-containing dendrimer 154 was directly synthesised.

![Dendrimer Structure](image)

**Table 2-7** ¹H NMR (400 MHz, CDCl₃), ¹³C NMR (100 MHz, CDCl₃) and HMBC data of dendrimer 150. Aside from C–Br, other quaternary carbons could not be assigned.

<table>
<thead>
<tr>
<th>Rings</th>
<th>Number</th>
<th>δ_H, ppm (multiplicity, J in Hz, integration)</th>
<th>δ_C, ppm</th>
<th>HMBC (¹H ↔ ¹³C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>7.08-7.12 (m, 9H)²</td>
<td>131.7</td>
<td>C-2</td>
</tr>
<tr>
<td></td>
<td>2/36</td>
<td>6.86-6.94 (m, 9H)²</td>
<td>128.1</td>
<td>C-34</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>6.86-6.94 (m, 9H)²</td>
<td>127.0</td>
<td>C-2</td>
</tr>
<tr>
<td>B</td>
<td>33/66</td>
<td>7.26 (s, 2H)</td>
<td>131.9</td>
<td>Quaternary carbons</td>
</tr>
<tr>
<td>C</td>
<td>7/11/40/44</td>
<td>7.19-7.23 (m, 6H)²</td>
<td>127.9</td>
<td>C-8 and C-9</td>
</tr>
<tr>
<td></td>
<td>8/10/41/43</td>
<td>7.08-7.12 (m, 9H)²</td>
<td>130.0</td>
<td>C-7 and C-9</td>
</tr>
<tr>
<td></td>
<td>9/42</td>
<td>7.19-7.23 (m, 6H)²</td>
<td>126.7</td>
<td>C-7 and C-8</td>
</tr>
<tr>
<td>D</td>
<td>14/18/47/51</td>
<td>7.08-7.12 (m, 9H)²</td>
<td>130.5</td>
<td>C-16</td>
</tr>
<tr>
<td></td>
<td>15/17/48/50</td>
<td>6.70 (dt, 2.4 and 8.4 Hz, 4H)</td>
<td>133.1</td>
<td>C-16</td>
</tr>
<tr>
<td></td>
<td>16/49</td>
<td>–</td>
<td>120.2</td>
<td>–</td>
</tr>
<tr>
<td>E</td>
<td>21/25/54/58</td>
<td>7.03 (dt, 2.4 and 8.4 Hz, 4H)</td>
<td>130.2</td>
<td>C-23</td>
</tr>
<tr>
<td></td>
<td>22/24/55/57</td>
<td>6.61 (dt, 2.4 and 8.4 Hz, 4H)</td>
<td>133.1</td>
<td>C-23</td>
</tr>
<tr>
<td></td>
<td>23/56</td>
<td>–</td>
<td>120.0</td>
<td>–</td>
</tr>
<tr>
<td>F</td>
<td>28/32/61/65</td>
<td>6.86-6.94 (m, 9H)²</td>
<td>127.3</td>
<td>C-29 and C-30</td>
</tr>
<tr>
<td></td>
<td>29/31/62/64</td>
<td>6.72-6.75 (m, 4H)</td>
<td>131.5</td>
<td>C-30</td>
</tr>
<tr>
<td></td>
<td>30/63</td>
<td>6.86-6.94 (m, 9H)²</td>
<td>126.1</td>
<td>C-28 and C-29</td>
</tr>
</tbody>
</table>

⁵Overlapping proton signals.

⁶Correlation to symmetrical carbons is represented by one of the carbons.

Table 2-7 ¹H NMR (400 MHz, CDCl₃), ¹³C NMR (100 MHz, CDCl₃) and HMBC data of dendrimer 150. Aside from C–Br, other quaternary carbons could not be assigned.
The $^1$H, $^{13}$C NMR and HMBC results for dendrimer 150 are shown in Table 2-7 as an example of the assignments performed. MALDI-TOF results confirmed the mass and isotope distribution pattern for this and the other dendrimers, and are shown in Appendix A.

**Figure 2-8** ORTEP drawing of symmetrical dendrimer 153. (a) and (b) Individual molecules in two different conformations; (c) Packing of the crystal.

**Figure 2-9** ORTEP drawing of symmetrical dendrimer 154. (a) and (b) Individual molecules in two different conformations; (c) Packing of the crystal.
Dendrimer 153 was crystallised from ethyl acetate/hexane solvent system, through vapour diffusion method (Figure 2-8). Another symmetrical pentaaryl dendrimer that has been crystallised was dendrimer 154, grown through the same solvent system and method (Figure 2-9). Both dendrimers crystallised as different conformers. Exhaustive analysis of these conformers will be discussed in Section 3.5 in Chapter 3.

The result for dendrimer 153 (Figure 2-8) showed that rings C and C’ were in a position very close to each other in crystal state. Upon further observation, it came to light that there were intermolecular Br···Br short contacts (Figure 2-10). On the other hand, the result for dendrimer 154 (Figure 2-9) showed that it crystallised as two conformers with $C_2$ symmetry, in which rings C and C’ were at the furthest from each other.

![Figure 2-10](image)

**Figure 2-10** (a) X-ray crystallography result; (b) the result drawn in 2D. Green: intermolecular short contacts between the peripheral bromines. Blue: short contacts with other molecules that are not shown here.

The distance between intermolecular Br···Br short contacts from the X-ray result was measured to be 3.560 Å, which is shorter than twice the distance of the van der Waals radius for Br ($r_{vdW}$ of Br = 1.85 Å; therefore the expected distance between Br ($d_{Br-Br}$) = 3.70 Å). This type of contact is known as halogen bonding, which is an attractive interaction driven by electrostatic force between a σ-hole of a covalently-bonded halogen and a negative site.
Similar to hydrogen bonding, halogen bonding also involves electrostatic interactions between an electron donor and an electron acceptor. Halogen may act as both the electron acceptor (halogen bond donor) and donor (halogen bond acceptor); or as the electron acceptor with N, S and O as the electron donor.\textsuperscript{91} In the case of dendrimer 153, the bromines act as both halogen bond donor and acceptor.

Politzer and co-workers suggested a theory known as the $\sigma$-hole theory to explain the interaction that results in halogen bonding. They explained that halogen bond occurs in an R–X bond because the one electron in the $p_z$ orbital of the halogen participates in the bond, leaving the outermost side of the $p_z$ lobe, which is directly opposite of the bond and not involved in the bond, lacking electron density and making it more electropositive. This electropositive side of the $p_z$ lobe surface is referred to as $\sigma$-hole. On the other hand, four electrons in $p_x$ and $p_y$ orbitals give rise to an electronegative ring around the sides of the halogen (Figure 2-11).\textsuperscript{92–94}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image}
\caption{The location of $\sigma$-hole and electronegative ring on a bromobenzene ring as well as experimental data obtained from X-ray crystallography.}
\end{figure}

The halogen is more polarisable when it is less electronegative, consequently making the $\sigma$-hole it creates more positive. The positivity of $\sigma$-hole and the strength of halogen bonds increases in the order F < Cl < Br < I.\textsuperscript{91} This means that fluorobenzene is less likely to form a halogen bond compared to bromobenzene.

In general, there are two types of halogen bond depending on the geometries of the atoms involved, Type I ($\theta_1 = \theta_2$) and Type II ($\theta_1 = \pm 180^\circ$, $\theta_2 = \pm 90^\circ$), where $\theta$ is the angle between C–X···Y or C–Y···X (Figure 2-12).\textsuperscript{91,95,96} Owing to the position of the $\sigma$-hole and the electronegative belt, the $\theta$ angle is close to 180$^\circ$ when the halogen acts as the halogen bond donor and close to 90$^\circ$ when it acts as the halogen bond acceptor.\textsuperscript{91} The angle of $\theta_1$ that is lower than 180$^\circ$ and close to 165$^\circ$ was argued to have stemmed from probability considerations, similar to that of hydrogen bonds.\textsuperscript{96}
All of these characteristic of halogen bonds were observed in the X-ray crystallography result of dendrimer 153. The halogen bond in this dendrimer is the Type II halogen bond with experimental $\theta_1$ and $\theta_2$ angles as well as the distance between the two bromine atoms ($d_{Br-Br}$) summarised previously in Figure 2-11.

Halogen bonding has been used in crystal engineering of solid state materials. It has also been observed to play important roles in biological activities such as the recognition of thyroid hormones (halogen bond between I···O) and as inhibitors against cancer targets. Owing to this useful applications, there are efforts that have been directed towards drug design that exploit the halogen bonding of the drug with proteins to increase its effectiveness.

The halogen bond in dendrimer 153 was thought to have been the cause that this dendrimer crystallised in a different fashion compared to dendrimer 154. The difference in the way this dendrimer crystallises in this example is an evidence of the presence of stereoisomers, albeit in the solid state. This will be described in detail in Chapter 3.

### 2.6.2 Synthesis of Pentaaryl Dendrimers Monoadducts

Two monoadducts of pentaaryl dendrimers have been synthesised as precursors to unsymmetrical dendrimers (Table 2-8). Br-CPD was chosen because the synthesis of this CPD is easier than F-CPD allowing scalability of reagent production as needed.

During the synthesis, a large amount of symmetrical dendrimer by-products was also formed. This was due to the terminal alkynes on both species possessing similar steric hindrance. Therefore, the core and the monoadduct competed with each other during the reaction and unwanted symmetrical dendrimer by-products were formed.
Purification of the products using flash column chromatography was difficult. When a small amount of sample was purified using preparative TLC, it was found that the separation was quite straightforward. To compensate for the formation of by-products, the syntheses were performed on several hundred milligram scale; therefore, preparative TLC was not an option. Separation using flash column chromatography could only be achieved with very non polar solvent systems.

### 2.6.3 Synthesis of Unsymmetrical Pentaaryl Dendrimers

The conversion of monooadducts to unsymmetrical pentaaryl dendrimers proved to proceed well. The monooadducts were heated in \( o \)-xylene to give the dendrimers in less than an hour, but the reactions were usually left overnight to ensure completion (Table 2-9).

#### Table 2-8 Synthesis of pentaaryl dendrimer monooadducts and their respective yields.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Ring A (R)</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>155</td>
<td>H</td>
<td>MonoPenta-H-Br</td>
<td>70</td>
</tr>
<tr>
<td>156</td>
<td>OH</td>
<td>MonoPenta-OH-Br</td>
<td>56</td>
</tr>
</tbody>
</table>

#### Table 2-9 Synthesis of unsymmetrical pentaaryl dendrimers and their respective yields.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Ring A (R)</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>157</td>
<td>H</td>
<td>Penta-H-Br-F</td>
<td>76</td>
</tr>
<tr>
<td>158</td>
<td>OH</td>
<td>Penta-OH-Br-F</td>
<td>90</td>
</tr>
</tbody>
</table>

It was initially thought that, because the difference between the left and right peripheries was only in the end groups (Br and F), only rings D, D’, E, E’ and the rings they are attached to (rings B and B’) would be magnetically inequivalent and that the rest of the
rings (rings A, C, C’, F and F’) would be magnetically equivalent because they belonged to different spin systems. However, when the $^{13}$C NMR spectra of these monoadducts were compared to their symmetrical analogues (Figure 2-13), it was apparent that rings C and F were not magnetically equivalent with rings C’ and F’ as each ring gave rise to their own $^{13}$C peaks.

This was similarly observed even in ring A that was the furthest from the peripheral moiety. This reveals that the difference in peripheral groups also affected these rings, making them magnetically inequivalent. Although each spin system is separated by rings B/B’, all the rings in the molecule acted like one big spin system. Therefore, when the symmetry was broken, the magnetic equivalency was also broken.

Of the two unsymmetrical dendimers, only 157 resulted in crystals with sufficient quality for X-ray crystallography. The crystal was grown through the vapour diffusion technique from ethyl acetate/hexane solvent system (Figure 2-14).

Similar to symmetrical dendrimer 154, this dendrimer also crystallises as two conformations in which rings C and C’ are at the furthest from each other. The only
difference is that since the symmetry has been broken, these two conformations no longer possess $C_2$ symmetry. Owing to the presence of fluorine on one side of the dendrimer, halogen bonding was not observed. More detailed analysis of the X-ray crystallography for this dendrimer and the symmetrical pentaaryl dendrimers is described in Chapter 3.

![ORTEP drawing of unsymmetrical dendrimer](image)

**Figure 2-14** ORTEP drawing of unsymmetrical dendrimer 157. (a) and (b) Individual molecules with two different conformations; (c) Packing of the crystal.

### 2.7 Synthesis of Hexaaryl Dendrimers

There are two types of hexaaryl dendrimers depending on the type of G/G’ rings: the parent-type and substituted hexaaryl dendrimers. The G/G’ rings in parent-type hexaaryl dendrimers are phenyl rings; whilst in substituted hexaaryl dendrimers they are substituted aromatic rings. Depending on the position of substituents, the substituted hexaaryl dendrimers can be further divided into *para*-substituted and *ortho*-substituted hexaaryl dendrimers (Figure 2-15).

The presence of rings G/G’ near the central region increases steric hindrance of hexaaryl dendrimers in comparison to pentaaryl dendrimers. As a result, the syntheses took, on average, about 14 days and in some cases even longer. Furthermore, the
presence of the rings leads to the formation of several stereoisomers, whose interconversion are more constrained. The stereoisomerism of hexaaryl dendrimers, their properties and resolution attempts are discussed further in Chapter 3.

**Figure 2-15** General structures of parent-type, para- and ortho-substituted hexaaryl dendrimers.

The presence of stereoisomers in hexaaryl dendrimers made full assignments of NMR spectra unfeasible. This, in addition to the large number of aromatic protons within all of the dendrimers, resulted in an overlap of signals in the $^1$H NMR spectra. The $^{13}$C NMR spectra yielded better data, particularly for the parent-type hexaaryl dendrimers, since the peaks could be differentiated to some extent, although full assignment was not possible. In the ortho-substituted hexaaryl dendrimers, the S/N ratio in $^{13}$C NMR spectra was poor, resulting in low-intensity peaks and making it difficult to differentiate between signal and noise. For all of the hexaaryl dendrimers, the structural proof was mainly obtained through mass spectrometry.

### 2.7.1 Synthesis of Symmetrical Hexaaryl Dendrimers

The symmetrical hexaaryl dendrimers were synthesised in good to excellent yields, except for one of the pyridyl-containing structures (Table 2-10). These dendrimers are interesting owing to their conformational complexity. The way each aromatic ring is positioned towards its neighbouring rings made the dendrimers exhibit stereoisomerism, creating different chemical environments particularly around central ring A. These are evident from various NMR spectra, described thoroughly in this section.
Among the parent-type hexaaryl dendrimers, the OH-containing 163 and 164 were synthesised through desilylation of their respective TBDMS-protected precursors 161 and 162. On the other hand, the OH-containing substituted hexaaryl dendrimers 167, 170 and 173 were synthesised through Diels-Alder reaction of their respective OH-containing cores.

Figure 2-16 shows the $^1$H NMR spectral comparison of all symmetrical parent-type dendrimers. In OTBDMS and OH-containing dendrimers, a doublet and a triplet can be observed at about 5.80 and 6.25 ppm respectively. The coupling constant of each peak is 1.2 Hz and integration reveals that the ratio of the doublet to the triplet is 2:1. The only protons that could give rise to peaks with such multiplicity, integration ratio and coupling constant were those that belong to the central ring A (Figure 2-17). 2D COSY spectra of these compounds showed a long-range correlation between the protons, confirming the idea. This assignment was further supported by 2D HMQC and HMBC data of the dendrimers. Similar peaks were observed in OH-containing pentaaryl dendrimers 153 and 154, with the doublet and triplet more downfield at about 6.35 and
6.65 ppm respectively, with similar coupling constant values.

Figure 2-16 From top to bottom: $^1\text{H}$ NMR spectra (400 MHz) comparison of dendrimers 159, 160, 161, 162, 163 and 164. The aliphatic region where TBDMS peaks appear are not shown for better clarity of the aromatic region. (●, ○ and ● = $^1\text{H}$ peaks of protons on ring A; □ = AB quartet, see main text)

Figure 2-17 $^1\text{H}$ peaks assignment on ring A of parent-type dendrimers.

In the hexaaryl dendrimers, these peaks appeared more upfield because rings C/C’ and G/G’ created an area with π-electron clouds and thus shielding the protons in ring A. The author refers to this area as the ‘pocket’; its effect is more pronounced in the substituted hexaaryl dendrimers, as will be discussed in the next section.

Due to the absence of phenolic C–O in dendrimers 159 and 160, the triplet peak shifted to a more downfield region, obscured within one of the aromatic envelopes. The doublet,
however, overlaps with another peak from the proton in ring A (labelled with yellow circle in Figure 2-17) and appeared as multiplet at about 6.28 ppm. This observation is supported by the 2D COSY result of these dendrimers.

One distinctive peak that appears in all of the parent-type dendrimers is the peak with a quartet-like pattern at about 6.15 ppm. Seeing the change of lineshape of the peak in all of the six parent-type dendrimers, and judging by the $\Delta \nu/J$ value of the peaks, the quartet-like peak is actually an AB quartet. The coupling constant ($J_{AB}$) value varies in each dendrimer but is on average about 7-8 Hz, suggesting an ortho relationship between A and B.

In an attempt to assign the AB quartet peak, several considerations were made:

- **Ring A**
  The protons in this ring are fully assigned (Figure 2-17) for all dendrimers and therefore the AB quartet does not belong to this ring.

- **Rings B/B’**
  These are fully substituted rings and therefore the AB quartet does not belong to this ring.

- **Rings D/E and D’/E’**
  HMBC spectrum does not show correlation between this $^1$H peak with the $^{13}$C peaks of either C–Br or C–F (ipso carbons) and therefore the AB quartet does not belong to this ring.

- **Rings F/F’**
  It is unlikely that the AB quartet belongs to this ring because the chemical enviroment of the protons in this ring should be similar.

- **Rings C/C’ and G/G’**
  It has been suggested that rings C/C’ and G/G’ create a pocket with $\pi$-electron cloud that shields ring A. The $\pi$-electron cloud in ring A in the pocket also contributes to shielding the nearby rings (rings C/C’ or G/G’), affecting their chemical environment, causing magnetic inequivalency among the protons on
those rings. Therefore, it is very likely that the AB quartet belongs to the protons of either of these rings. Protons that are facing towards the pocket (inwards) give rise to the AB quartet (Figure 2-18).

**Figure 2-18** One conformation in dendrimer 159 where the pockets are formed by rings A, C' and G. The protons pointing towards the pocket (red) come from rings C and G'; on the other side of these rings are the protons pointing away from the pocket (blue).

Although this looks peculiar at this point, the NMR spectra of the substituted hexaaryl dendrimer would later support the idea, which is discussed in the latter part of this section. No other information could be obtained from the $^1$H NMR spectra of the above dendrimers because the rest of the peaks were obscured within the aromatic envelope.

**Figure 2-19** By-products (174 and 175) that were formed during the synthesis of 163.

During the synthesis of dendrimer 163, two unexpected by-products were obtained (Figure 2-19). FTIR of both showed the absence of aliphatic TBDMS band and OH absorption band, suggesting desilylation had taken place but the free hydroxy reacted further to form these by-products. Upon NMR characterisation it was found that the first by-product (174) was dendrimer 163 with a fluoromethylene group attached and was isolated in 29% yield. The second by-product (175) was a dimerisation of dendrimer
with a methylene group bridging the two dendrimer molecule, isolated in 14% yield. The desired dendrimer 163 itself was only formed in 36% yield, suggesting that most of the dendrimer had formed by-products.

The presence of fluorine in dendrimer 174 was confirmed by $^1$H, $^{13}$C, $^{19}$F NMR and HMBC. $^1$H and $^{13}$C NMR spectra of 174 showed a doublet peak at 4.66 ppm ($^2$J$_{\text{H-F}} = 55.0$ Hz) and 101.8 ppm ($^1$J$_{\text{C-F}} = 216.3$ Hz), respectively, which belong to the methylene group. The $^1$H-coupled $^{19}$F NMR spectrum (Figure 2-20 (a)) showed a peak -146.0 ppm (t, $^2$J$_{\text{H-F}} = 55.0$ Hz), further confirming the presence of fluorine as well as its position on the methylene group. Unfortunately, the $J_{\text{C-F}}$ value could not be determined from the $^{19}$F NMR since the $^{13}$C-satellite was not observable due to the low S/N ratio, even when $^1$H-decoupled $^{19}$F NMR had been performed (Figure 2-20 (b)). Nonetheless, phenolic carbon appeared as a doublet at 155.3 ppm, suggesting long range $^{13}$C–$^{19}$F coupling ($^3$J$_{\text{C-F}} = 3.5$ Hz). This was also supported by the fact that the $^1$H and $^{19}$F NMR data and $^1$H–$^{19}$F coupling constant for the methylene group were similar to those reported for (fluoromethoxy)benzene$^{99,100}$ and its substituted derivatives.$^{101}$

![Figure 2-20](image_url) $^{19}$F NMR spectra (376 MHz) of by-product 174. (a) $^1$H-coupled, showing the splitting due to heteronuclear $^1$H–$^{19}$F coupling, and (b) $^1$H-decoupled.

The formation of dendrimer 175 was confirmed by $^1$H and $^{13}$C NMR which show the presence of methylene group at 3.66 (s, 2H) and 94.6 ppm, respectively, in addition to comparison of integral ratio between the methylene protons and the aromatic protons. The one bond $^1$H–$^{13}$C relationship was confirmed by 2D HMQC, while correlation of the methylene proton to the phenolic carbon was confirmed by 2D HMBC.
Both by-products have one common functional group, which is the methylene group. The formation of the by-products was thought to have been caused by CH$_2$Cl$_2$ during the extraction work-up (Scheme 2-17). The fluorine in compound 174 was thought to have come from TBAF used during deprotection.

![Scheme 2-17 Proposed mechanism for the formation of by-products 174 and 175.](image)

To prevent the formation of these by-products, CH$_2$Cl$_2$ was avoided in all TBDMS deprotection reactions with TBAF and Et$_2$O was used instead during the extraction work-up. The only drawback was that a larger quantity of Et$_2$O was required due to the slightly low solubility of the dendrimers. Changing the organic phase to diethyl ether proved to be effective since no similar by-products were observed in other desilylation reactions. When the synthesis of dendrimer 163 was repeated and Et$_2$O was used, 96% yield was achieved and formation of by-products was not observed.

Three pyridyl-containing hexaaryl dendrimers (165, 166 and 167) were synthesised. The OH-containing analogue, Hexa-OH-(2-Pyridyl)-Br-Br (dendrimer 167), was synthesised through Diels-Alder reaction, because the yield of MEM deprotection reaction was poor. The purification of these dendrimers, particularly 167, was difficult and some impurities remained even following several purification attempts.

Evidence that the pyridyl-containing dendrimers had been successfully synthesised was obtained through MALDI-TOF mass spectrometry because the $^1$H spectra of the dendrimers gave broad and overlapping peaks, while the $^{13}$C NMR spectra suffered from a poor low S/N ratio.

Initially, the line broadening in the $^1$H NMR spectra of these dendrimers was thought to be due to the aggregation of the molecules in solution. Similar broadening behaviour in
NMR spectra has been observed in hexa-\textit{peri}-hexabenzocoronene derivatives, which aggregated in solution due to strong $\pi$–$\pi$ stacking interactions.\textsuperscript{102} Such aggregation would be resolved by measuring the NMR spectra at more dilute concentration.\textsuperscript{103}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2-21}
\caption{\textsuperscript{1}H NMR spectrum (400 MHz) of \textbf{165} as well as the spectra of the diluted samples.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2-22}
\caption{DEPT90 spectrum (top, 100 MHz) and $^{13}$C NMR spectrum (bottom, 100 MHz) comparison of dendrimer \textbf{165}. (\textbullet{} = Ar $\text{C}$–Br; = Ar $\text{CH}$=N–; = other quaternary $^{13}$C)}
\end{figure}
Aiming to resolve this, dilution experiments (Figure 2-21) were performed by diluting the initial sample to 10, 25, 100 and 200 times the initial concentration and subsequently recording the \(^1\text{H}\) NMR of each sample. Changes in line shape could clearly be observed as the sample became more dilute, which is indicative of aggregation. Even at 200 times dilution however, the \(^1\text{H}\) NMR spectrum of 165 was still unresolvable; therefore, the peak broadening was likely not caused by the aggregation of the dendrimer in solution.

In the parent-type dendrimers, 35 mg of sample was usually enough to give well-resolved peaks with high S/N ratio in the \(^{13}\text{C}\) NMR spectrum. Unfortunately, the \(^{13}\text{C}\) NMR spectrum of 165 showed poorly-resolved peaks with low S/N ratio despite using more sample. It was found that the resolution (FIDRES) parameter was set to about 0.46 Hz (which corresponds to 0.0046 ppm) and therefore should have been able to resolve the peaks roughly separated by that amount of shift difference. The distortion enhancement by polarisation transfer (DEPT) experiment is known to have several times greater sensitivity compared to the routine \(^{13}\text{C}\) NMR. The DEPT90 result showed better S/N ratio and slightly better resolution at the expense of losing the quaternary \(^{13}\text{C}\) peaks. Unfortunately, the peaks were still unresolvable (Figure 2-22).

The only reason that can explain these observations is the presence of stereoisomers in the sample. These isomers are distinguishable in NMR and therefore the \(^1\text{H}\) NMR peaks appeared as overlapping and broad peaks whilst the \(^{13}\text{C}\) NMR became unresolvable. The low S/N ratio of the \(^{13}\text{C}\) peaks can also be explained since only a small amount of each isomer is present in the sample (less than 50 mg per isomer). The cause of these isomers is the position of the nitrogen within the pyridyl rings that makes the G/G'-rings axes chiral. These axes have previously been shown in bold red in Figure 2-7.

In order to fully investigate the stereoisomers, an attempt to synthesise \(^{15}\text{N}\)-enriched pyridine starting material and to investigate the resulting dendrimer using \(^{15}\text{N}\) NMR was proposed. Unfortunately reagents were not commercially available. Therefore, fluorine-containing dendrimers were synthesised instead, because they were deemed to be the closest analogue that possessed NMR active nuclei.

Figure 2-23 summarises the symmetrical fluorine-containing dendrimers that were synthesised in this research. The position of the fluorine was premeditated so that the resulting fluorine-containing dendrimers could mimic both parent-type dendrimers and
pyridyl-containing dendrimers.

![Dendrimer structures](image)

**Figure 2-23** Fluorinated *para*-substituted and *ortho*-substituted dendrimers. The *para*-substituted dendrimers represent the parent-type dendrimers whilst the *ortho*-substituted dendrimers represent the pyridyl-containing dendrimers.

Fluorine’s naturally occurring isotope ($^{19}$F) has high abundance (100%) and high sensitivity in NMR (0.83 relative to $^1$H),\(^{104}\) making it the second most sensitive nucleus after $^1$H. Fluorine is also commonly used as a substitute of hydrogen due to its small size,\(^{89}\) and therefore the fluorine-substituted structure does not incur a large additional steric penalty. By using $^{19}$F as the reporter nucleus and measuring the $^{19}$F NMR of the stereoisomer mixture, it is possible to identify the chemical environment of the fluorines in each isomer without affecting much of the steric aspect of the entire structure.

The synthesis of *para*-substituted dendrimers gave moderate to excellent yields (Table 2-10). As previously expected, the $^1$H and $^{13}$C NMR results of *para*-substituted dendrimers yielded peaks with similar profiles to parent-type dendrimers. Aside from the routine $^1$H NMR characterisations, $^{19}$F-decoupled $^1$H NMR experiments were also performed to these dendrimers in order to observe the $^1$H peaks that are on the fluorobenzene ring. The $^1$H NMR ($^{19}$F-coupled and $^{19}$F-decoupled) results of dendrimers 168 and 169 are shown in Figure 2-24.

The peak that appeared at about 6.28-6.34 ppm resembled the ones previously observed in parent-type dendrimers (dendrimers 159 and 160, Figure 2-16). This peak was determined to belong to ring A of dendrimers 168 and 169, representing the same protons as previously discussed for parent-type dendrimers.

Several peaks outside the aromatic envelope can be observed in the $^1$H NMR spectra with the most upfield peak at about 5.69 ppm for both dendrimers. Since dendrimers
168, 169 and 170 are similar, only dendrimer 168 was fully studied, although some results from dendrimer 169 would help in the latter part of the study. The results from dendrimer 168 also apply to dendrimers 169 and 170 due to the structural similarity.

![Figure 2-24](image)

The peaks labelled by red circles originate from the central fluorobenzene rings (rings G/G’) in both dendrimers 168 and 169, but it was difficult to establish where on the fluorobenzene rings these protons are. The position of these protons relative to the fluorine on the fluorobenzene rings, could be determined by identifying the heteronuclear $^1$H–$^{19}$F coupling constant values. Owing to the presence of homonuclear $^1$H–$^1$H couplings however, the heteronuclear $^1$H–$^{19}$F coupling was obscured and the coupling constant value was difficult to be determined unambiguously.

To overcome this problem, an NMR experiment, in which the homonuclear $^1$H–$^1$H couplings had been eliminated, was performed. This experiment, known as the Pure Shift NMR, results in a spectrum where only the heteronuclear $^1$H–$^{19}$F couplings are revealed and their coupling constant values can be unambiguously determined without the interference of homonuclear $^1$H–$^1$H couplings.
There are several homonuclear broadband decoupling methods known to date, but the ones used in this research were Pure Shift Yielded by Chirp Excitation (PSYCHE) and Bilinear Rotational Decoupling (BIRD). PSYCHE, known to have the highest sensitivity, was used to obtain 1D Pure Shift NMR spectra; whilst BIRD is known to have high sensitivity in obtaining 2D Heteronuclear Single Quantum Correlation (HSQC) spectra. The application of 1D Pure Shift NMR to reveal heteronuclear couplings has previously been demonstrated by Aguilar and co-workers to also reveal heteronuclear $^1$H–$^{19}$F couplings in simple organic molecules.

Due to the presence of stereoisomers in the sample, Pure Shift NMR could not fully resolve the aromatic envelope. Furthermore, it resulted in low S/N ratio making it difficult to determine the heteronuclear $J_{H,F}$ values (Figure 2-25 and Figure 2-26). $^{19}$F-decoupled Pure Shift NMR experiment confirmed that the protons of interest were coupled to the $^{19}$F nuclei.

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1D PSYCHE Pure Shift NMR and 2D BIRD HSQC experiments in this thesis were performed either by the author, Dr Matthew Cliff, Senior Experimental Officer, The University of Manchester or Dr Ralph Adams, Research Fellow in NMR Spectroscopy, Morris Group, The University of Manchester.
Figure 2-26 A portion of the spectra is enlarged to show the low S/N ratio of one of the peak in the Pure Shift NMR spectrum. (● = 19F-coupled 1H peaks)

Owing to this difficulty, a 2D $^1$H–$^{13}$C BIRD HSQC experiment was performed. This experiment was carried out to determine not only the heteronuclear $J_{\text{H-F}}$ values, but also the heteronuclear $J_{\text{C-F}}$ values of the peaks labelled with red circles. Therefore, the heteronuclear coupling constant values were not obtained solely from coupling with the $^1$H nuclei but also by coupling with the $^{13}$C nuclei. Furthermore, the 2D experiment also revealed the other $^1$H and $^{13}$C couplings with $^{19}$F nuclei on the fluorobenzene ring that were hidden under the aromatic envelope and were not directly seen in both 1D $^1$H NMR and 1D Pure Shift NMR. This method has been used previously by Wong and co-workers during the structural elucidation of various fluorinated compounds.\textsuperscript{109–111}

The BIRD sequence in the HSQC is used to suppress the proton signals originating from those bound to $^{12}$C nuclei.\textsuperscript{105,107,112} Therefore, the protons that give rise to the peaks in the spectrum are only the protons that are bound to $^{13}$C nuclei. Owing to the low abundance of $^{13}$C nuclei (~1.1%), the probability of two $^{13}$C nuclei being adjacent to each other is very low and thus results in Pure Shift NMR in the proton dimension. In 2D HSQC the BIRD sequence is particularly favourable because it only observes the protons that are coupled to $^{13}$C nuclei, therefore the resulting spectrum is free of coupling artefacts and sensitivity penalty due to the decoupling scheme.\textsuperscript{105,112}
In practice, it was difficult to determine which peaks in the HSQC spectra were coupled to $^{19}$F nuclei since there were a large number of correlation peaks in the spectrum that appeared very close to each other. Therefore, to assist in this determination, 2D $^{19}$F-decoupled $^1$H–$^{13}$C BIRD HSQC was also performed (Figure 2-27 (a)) in conjunction to the normal 2D BIRD HSQC.

**Figure 2-27** A pair of $^1$H–$^{13}$C BIRD HSQC correlation peaks. (a) $^{19}$F-coupled peaks in both dimensions (blue) collapses into a pair of adjacent peaks (red) in the $^{19}$F-decoupled spectrum (decoupling was performed to the F1 dimension); (b) Determination of heteronuclear $J_{H-F}$ and $J_{C-F}$ values from the correlation peak. (F2 = Pure Shift NMR, F1 = $^{13}$C NMR)

The decoupling was performed to the indirect dimension (F1 dimension, $^{13}$C NMR) and the result was stacked onto the $^{19}$F-coupled HSQC spectra. The pairs of peaks that collapsed into two adjacent peaks in the F2 dimension were those originated from the $^1$H and $^{13}$C coupled to the $^{19}$F nuclei, as shown in Figure 2-27 (a). After all of the $^{19}$F-coupled peaks had been accounted for, the heteronuclear coupling constants ($J_{H-F}$ and $J_{C-F}$) were determined from the $^1$H and $^{13}$C chemical shift information obtained from the correlation peaks, as exemplified in Figure 2-27 (b). This method has been used by Guo and Wong to determine the heteronuclear coupling constant values of several fluorine-containing organic compounds.

Guo and Wong reported the values of $^1$H–$^{19}$F and $^{13}$C–$^{19}$F coupling constant in several fluorinated aromatic compounds as well as the position of the protons and carbons relative to the fluorine. For the para system, compound 4-fluorobiphenyl (176) was
used as a reference. The $J_{HF}$ and $J_{CF}$ values of the protons and carbons on the fluorobenzene ring in dendrimer 168 were compared to the $J_{HF}$ and $J_{CF}$ values of 176 to determine the position. Table 2-11 summarises the experimental $J_{HF}$ and $J_{CF}$ values obtained from the 2D $^1$H–$^{13}$C BIRD HSQC result for dendrimer 168 (Figure 2-28). The experiment and analysis were also performed to dendrimer 170 and the results are summarised in Appendix B.

**Figure 2-28** (a) 2D $^1$H–$^{13}$C BIRD HSQC spectrum (500 MHz) for dendrimer 168, (b) *ortho* region and (c) *meta* region of the fluorobenzene rings. (F2 = Pure Shift NMR, F1 = $^{13}$C NMR)
The most upfield proton in the spectra, originated from a proton on the fluorobenzene rings, formed a pocket which increases shielding by the reference to fluorine.

Table 2-11 Experimental $J_{HF}$ and $J_{CF}$ values obtained from 2D $^1$H-$^1$C BIRD HSQC (500 and 125 MHz) spectrum for dendrimer 168. Compound 4-fluorobiphenyl (176) is used as a reference to determine the position of the protons and carbons on the ring.

These data reveal that the aromatic proton peak that appeared at 5.68 ppm (Table 2-11, entry 5), which was the most upfield proton in the spectra, originated from a proton on the meta position to the fluorine in the fluorobenzene ring. Similar to what was previously observed in the parent-type hexaaryl dendrimers, rings A, C/C’ and G/G’ formed a pocket which increases shielding by the $\pi$-electron cloud of the aromatic rings (Figure 2-29) and therefore this protons appeared at the most upfield region.

Figure 2-29 One of several possible conformations in dendrimer 168. Some of the protons on the fluorobenzene rings are pointing towards (red) and away (blue) from the pocket. Note that this conformation possesses $C_2$ symmetry.

The chemical shifts of the peaks and their respective coupling constants obtained are strong evidence towards the presence of the pocket. They indicate how the protons pointing inwards exist in a different chemical environment than those pointing outwards, even when they are on the same ring. This supports the model previously suggested in the parent-type hexaaryl dendrimer.
Table 2-11 also shows that there are three other *meta* protons on rings G/G’. The protons at the more downfield region (entry 7 and 8) were likely to be pointing away from the pocket; the same applies for the *ortho* protons. Therefore, one fluorobenzene ring possesses two *meta* and two *ortho* protons that are distinguishable from one another owing to the presence of the pocket. There are four *meta* and four *ortho* protons according to the results, which means there should be two distinguishable fluorobenzene rings present in the sample. Since the conformation shown in Figure 2-29 possesses $C_2$ symmetry, there should exist another conformation that also possesses symmetry that gives rise to the other pair of *meta* and *ortho* protons. This result suggests that there are two species that are distinguishable by NMR; this will be discussed further and supported with other spectroscopic data in Chapter 3.

2D $^1$H–$^1$H TOCSY was performed to provide support for this proposal. Important spin-spin correlation information is listed below.

- The most upfield proton at 5.68 ppm (Table 2-11, *meta*, entry 5) correlates with the peaks at 6.45 (*ortho*, entry 1), 6.59 (*ortho*, entry 3) and 6.69 ppm (*meta*, entry 7) suggesting that they belong to one fluorobenzene ring.
- The proton at 6.14 ppm (Table 2-11, *meta*, entry 6) correlates with the peaks at 6.56 (*ortho*, entry 2), 6.68 (*ortho*, entry 4) and 6.77 ppm (*meta*, entry 8) also suggesting that they belong to one fluorobenzene ring. The fact that this fluorobenzene ring contains protons with differing chemical shifts suggests that this is a different fluorobenzene ring from the one described above. Other spectroscopic data later reveal that both fluorobenzene rings belong to two different and distinguishable stereoisomers (Chapter 3).

Aside from the $^{19}$F-coupled $^1$H peaks, the $^1$H NMR spectra of 168 (Figure 2-24) showed several broad doublets at 6.12, 6.51 and 6.80 ppm that are not coupled to $^{19}$F nuclei. Making use of the informations gathered thus far, it can be suggested that these doublets are AX quartets, and that they belong to rings C/C’. 2D COSY experiment showed a correlation between the peaks at 6.12 and 6.80 ppm with coupling constant value ($J_{AX}$) of 7.7 Hz suggesting *ortho* relationship between the two peaks. Unfortunately, the peak at 6.51 ppm correlated with another peak that was obscured within a multiplet between 6.83-6.93 ppm. The AX coupling constant value can still be obtained from that peak alone ($J_{AX} = 7.7$ Hz) but this value could not be compared with its pair for confirmation. 2D Total Correlation Spectroscopy (TOCSY) revealed all of the spins that these peaks
were coupled to each other in their respective spin system and confirmed the assignment.

Combining all of the information, the $^1$H NMR assignment of dendrimer 168 could be performed, as shown in Figure 2-30 below.

![Figure 2-30](image)

**Figure 2-30** Assigned $^1$H NMR spectrum (500 MHz) of dendrimer 168. Each ring is colour coded and represented by only one side (e.g. rings C/C' are represented by ring C only) for clarity. The subscripts 1 and 2 represent distinguishable stereoisomers 1 and 2. Positions of protons on the ring are coded with i, ii, iii for ring A and o, m, p for the rest of the rings relative to the substituent with higher priority. For rings affected by the presence of pockets (rings C/C' and G/G') the positions of the substituents are further distinguished by subscripts i and ii, with i being the substituents facing towards the pocket and ii being the substituents facing away from the pocket. The integral values are not doubled to better observe the ratio between each peaks.

In dendrimer 170 (Hexa-OH-(4-Fluorophenyl)-Br-Br), the presence of a hydroxy group on ring A resulted in the protons ortho and para to the hydroxy appearance at shielded chemical shifts. The same observation was also previously seen in OTBDMS- and OH-containing parent-type dendrimers (Figure 2-16) as doublet and triplet. In 170, the doublet and triplet were observed as a doublet of doublet ($dd$) and a doublet of triplet ($dt$), respectively. The $^1$H NMR, $^{19}$F-decoupled $^1$H NMR, Pure Shift NMR and $^{19}$F-decoupled Pure Shift NMR of 170 are shown Figure 2-31.

Since the $dd$ and $dt$ peaks on ring A did not collapse into one singlet each in the Pure Shift NMR, it was concluded that they were not $dd$ and $dt$ but two doublets and two
triplets. Consequently, this means that they originated from two species, with each species giving rise to one doublet and one triplet. Although this dendrimer is structurally similar to the parent-type, the presence of fluorines on rings $G/G'$ has created a different chemical environment for the protons on ring A to become distinguished.

![Figure 2-31](image)

*Figure 2-31* From top to bottom: $^1$H NMR, $^{19}$F-decoupled $^1$H NMR, Pure Shift NMR, $^{19}$F-decoupled Pure Shift NMR spectra (500 MHz) of dendrimer 170. (● = $^{19}$F-coupled $^1$H peaks; ▲ = $^1$H peaks not coupled to $^{19}$F nuclei; ■ = $^1$H peaks ortho to the hydroxy group in ring A; □ = $^1$H peaks para to the hydroxy group in ring A)

The $^{19}$F NMR ($^1$H-decoupled) spectrum of dendrimer 168 showed that there are two $^{19}$F peaks (Figure 2-32), even though the dendrimer is symmetrical. This indicates that there were at least two distinguishable stereoisomers, and therefore suggests the presence of stereoisomers in the parent-type dendrimers as well.

The $^{19}$F NMR result of dendrimer 170 is not shown; however it also showed two peaks similar to that of dendrimer 168. This result supports what was observed in $^1$H NMR of dendrimer 168 and 170: all evidence points towards the presence of two distinguishable stereoisomers. This will be explained in more detail in Chapter 3.
The $^{19}$F NMR spectrum ($^1$H-decoupled, Figure 2-33) for dendrimer 169 showed the presence of six peaks. Upon comparing this result with dendrimer 168, it was clear that the peripheral fluorine peaks came up between the central fluorine peaks. This result and this comparison method have greatly assisted $^{19}$F peak identification of various other analogues in the latter stages this research.

The synthesis of ortho-substituted dendrimers gave good to excellent yields. The $^1$H NMR results of ortho-substituted dendrimers showed a large aromatic envelope due to overlapping peaks, but the spectra were more defined than those of the pyridyl-containing dendrimers. The $^{13}$C NMR spectra, however, were similar to the pyridyl-containing dendrimers with peaks appearing broad with low S/N ratio.

There were three main ortho-substituted dendrimers that were synthesised: dendrimers 171, 172 and 173. Since 172 and 173 are structurally similar to 171, the one that was
fully investigated was dendrimer 171. The results for this dendrimer can also be applied to 172 and 173.

The comparison of $^1$H NMR, $^{19}$F-decoupled $^1$H NMR, Pure Shift NMR and $^{19}$F-decoupled Pure Shift NMR spectra of 171 is shown in Figure 2-34. A set of four shielded peaks were observed at about 5.30-6.20 ppm. Based on the results obtained from the para-substituted dendrimer, it was proposed that these protons were the ones that sat inside the pocket between two aromatic rings. The only peak in this set that changed multiplicity when $^{19}$F-decoupling was performed was the least shielded peak. This suggests that this peak belonged to the fluorobenzene ring (rings G/G’) while the rest of the peaks in this set belonged to rings C/C’.

Several other peaks were observed around 6.00-6.52 ppm, some of which were coupled to fluorine. Owing to the presence of stereoisomers, a large and unresolvable aromatic envelope ranging from about 6.55-7.15 ppm was observed. Aside from the aforementioned peaks, no other peaks provided useful information since most of them were obscured within the aromatic envelope.
As observed in Figure 2-34, Pure Shift NMR did not manage to resolve the aromatic envelope due to the large number of signals. Although the S/N ratio was fairly good for some peaks, it was not possible to determine the heteronuclear $J_{\text{H-F}}$ values by relying on the Pure Shift NMR alone, as previously encountered with the para-substituted dendrimer 168 (Figure 2-25 and Figure 2-26).

Figure 2-35 2D $^1\text{H}$–$^{13}\text{C}$ BIRD HSQC spectrum (500 and 125 MHz) for dendrimer 171. (F2 = Pure Shift NMR, F1 = $^{13}\text{C}$ NMR)

Similar to the para-substituted dendrimer 168, dendrimer 171 was subjected to 2D $^1\text{H}$–
\(^{13}\)C BIRD HSQC to obtain the heteronuclear \(J_{\text{H-F}}\) and \(J_{\text{C-F}}\) values and determine the positions of the peaks on the fluorobenzene ring. Owing to the position of the fluorine on the ring, the value of \(J_{\text{C-F}}\) was also necessary to determine the exact position of the protons and carbons on the fluorobenzene ring, which made the HSQC measurement even more important (Figure 2-35). The experiment and analysis were also performed to dendrimer 173 and the results are summarised in Appendix B.

![Diagram of fluorobenzene ring with peak positions and J values](image)

<table>
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<tr>
<th>No</th>
<th>(^{1})H Chemical shift ((\delta), ppm)</th>
<th>(^{13})C Chemical shift ((\delta), ppm)</th>
<th>(J_{\text{H-F}}) (Hz)</th>
<th>(J_{\text{C-F}}) (Hz)</th>
<th>Position relative to fluorine</th>
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<td>2.9</td>
<td>meta (5)</td>
</tr>
<tr>
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<td>6.20</td>
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<td>7.9</td>
<td>3.7</td>
<td>meta (5)</td>
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<td>133.0</td>
<td>5.9</td>
<td>3.7</td>
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<td>133.4</td>
<td>5.9</td>
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<td>132.7</td>
<td>7.8</td>
<td>3.7</td>
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</tr>
<tr>
<td>27</td>
<td>6.97</td>
<td>133.0</td>
<td>5.9</td>
<td>4.4</td>
<td>meta (5)</td>
</tr>
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Table 2-12 Experimental \(J_{\text{H-F}}\) and \(J_{\text{C-F}}\) values obtained from 2D \(^{1}\)H–\(^{13}\)C BIRD HSQC (500 and 125 MHz) spectrum for dendrimer 171. Compound 2-fluorobiphenyl (177) is used as a reference compound\(^{13}\) to determine the position of the protons and carbons on the ring.

Two 2D \(^{1}\)H–\(^{13}\)C BIRD HSQC experiments, \(^{19}\)F-coupled in both dimensions and \(^{19}\)F-decoupled in the indirect dimension, were performed. The results were then compared
and the peaks that were coupled to $^{19}$F nuclei were established. The $J_{H-F}$ and $J_{C-F}$ values were then determined and compared to the values in 2-fluorobiphenyl (177)\textsuperscript{111} to assign the position of the protons and carbons on the fluorobenzene ring. Table 2-12 summarises the proton and carbon peaks, their $J_{H-F}$ and $J_{C-F}$ values, as well as their position on the fluorobenzene ring.

It was difficult to determine the $J_{H-F}$ value for the peaks belonging to the proton \textit{para} to fluorine (Table 2-12, entry 8-14) because the coupling constant value was small (0.3-1.5 Hz).\textsuperscript{111} The $J_{C-F}$ values of these carbons were similar to the $J_{C-F}$ values for the carbons on the \textit{meta} position (Table 2-12, entry 21-27). However, since the $J_{H-F}$ on the \textit{meta} position was observable, the protons and carbons on the \textit{para} position could be determined by elimination based on the $J_{C-F}$ values.

Figure 2-36 (below) shows that the $^{19}$F NMR ($^1$H-decoupled) spectrum of dendrimer 171 gave eight peaks. This proves that there were several stereoisomers in this dendrimer. By having \textit{ortho} substituents in its structure, this dendrimer is able to mimic the pyridyl-containing dendrimer 165-167. Therefore the $^{19}$F NMR result for dendrimer 171 also indicates that it was very likely that stereoisomers were present in the pyridyl-containing dendrimers.

The $^{19}$F NMR spectrum for 172 also showed the same eight peak pattern for the central fluorines. The peripheral fluorines appeared more upfield (about -117.0) as overlapping singlets (Figure 2-37). This indicates that the chemical environment of the peripheral region is different for each stereoisomer, even though it is several bonds away from the central region where the chiral axes are present.
Figure 2-37 $^{19}$F NMR spectrum (1H-decoupled, 470 MHz) of dendrimer 172.

The details of the stereoisomer conformations and assignments of the ortho-substituted dendrimers are described in more detail in Chapter 3.

2.7.2 Synthesis of Hexaaryl Dendrimers Monoadducts

Similar to the synthesis of unsymmetrical pentaaryl dendrimers, synthesis of unsymmetrical hexaaryl dendrimers was also performed in two stages. The first stage was the synthesis of the monoadduct and the second stage was the conversion of monoadducts to unsymmetrical dendrimers.

Even though the monoadducts of hexaaryl dendrimers seem to possess large steric hindrance around the central area when compared to the pentaaryl monoadducts, substantial amounts of symmetrical dendrimer by-products were formed during the synthesis of monoadducts. This resulted in low yields during the synthesis of these monoadducts, even when using excess core (1.5 equiv.). The general scheme for the synthesis of monoadducts as well as the yields are shown in Table 2-13.

Purification of monoadducts was difficult and could only be achieved through either preparative TLC or preparative reverse-phase HPLC. Column chromatography failed to separate the monoadducts from the diadduct by-products and the excess starting material (core). Purification of monoadducts 178, 179, 180 and 182 was achieved by preparative TLC; multiple attempts to purify 181 with preparative TLC failed, and it had to be repurified with reverse-phase HPLC. Similarly, monoadduct 183 required reverse-phase HPLC purification as no solvent system could be found for preparative TLC purification.
The fluorine-containing monoadducts in general have two different regions, where the fluorobenzene ring is attached. The region where it is attached to the alkyne is called the outer region, whereas the region where it belongs to the hexaaryl moiety is called the inner region. Aside from these regions, these monoadducts also possess chiral axes; the para-system monoadducts possess one chiral axis while the ortho-system possesses two chiral axes.

Figure 2-38 shows the difference between the two regions as well as the chiral axes in the monoadducts. The outer region is shown with the red, while the inner region is shown with green fluorobenzene rings. The fluorines in these two regions give rise to distinct $^{19}$F peaks at different chemical shifts in the $^{19}$F NMR spectra.

Table 2-13 Synthesis of hexaaryl dendrimers monoadducts.

<table>
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<tr>
<th>Comp. No.</th>
<th>Ring A (R)</th>
<th>Rings G/G' (Ar)</th>
<th>Name</th>
<th>Yield (%)</th>
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<td>H</td>
<td>Phenyl</td>
<td>MonoHexa-H-Phenyl-Br</td>
<td>29</td>
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<td>OTBDMS</td>
<td>Phenyl</td>
<td>MonoHexa-OTBDMS-Phenyl-Br</td>
<td>46</td>
</tr>
<tr>
<td>180'</td>
<td>H</td>
<td>4-Fluorophenyl</td>
<td>MonoHexa-H-(4-Fluorophenyl)-Br</td>
<td>27</td>
</tr>
<tr>
<td>181</td>
<td>OH</td>
<td>4-Fluorophenyl</td>
<td>MonoHexa-OH-(4-Fluorophenyl)-Br</td>
<td>60</td>
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<td>182'</td>
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<tr>
<td>183</td>
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<td>2-Fluorophenyl</td>
<td>MonoHexa-OH-(2-Fluorophenyl)-Br</td>
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</tbody>
</table>

$^{a}$ These monoadducts were synthesized in conjunction with J. Mistry, Gardiner group.

$^{19}$F NMR characterisations were performed only on the fluorine-containing monoadducts 180-183. Interesting peaks were observed in the $^{19}$F NMR spectra of these monoadducts, particularly of the ortho-systems 182 and 183.
The $^{19}$F NMR spectra of the para-system monoadducts 180 and 181 are shown in Figure 2-39. The red and green triangles in the picture above represent the fluorines in the outer and inner regions, respectively. This assignment was made on the basis that the fluorines in the outer region would not be shielded by any nearby aromatic rings. This was further supported by comparison of spectra of fluorine-containing cores with the spectra of fluorine-containing monoadducts.

The $^{19}$F NMR spectra (Figure 2-40) of the ortho-system monoadducts 182 and 183 gave rise to a similar pattern, but with more peaks at each region because they possess two chiral axes. The chiral axes resulted in more stereoisomers and hence, more peaks in the $^{19}$F NMR. This further supported by other spectroscopic data explained in Chapter 3.
2.7.3 Synthesis of Unsymmetrical Hexaaryl Dendrimers

The syntheses of unsymmetrical hexaaryl dendrimers were carried out by heating the
monoadducts with F-CPD in o-xylene at high temperature (200 °C). The yield of this
reaction ranged from moderate to very good (Table 2-14). Since all of these dendrimers
possess fluorines on the peripheral region, the term fluorine-containing dendrimers only
applies to those possessing central fluorines.

![Image of synthesis diagram]

**Table 2-14** Synthesis of unsymmetrical hexaaryl dendrimers.

<table>
<thead>
<tr>
<th>No.</th>
<th>Ring A (R)</th>
<th>Rings G/G' (Ar)</th>
<th>Name</th>
<th>Yield (%)</th>
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<tr>
<td>184</td>
<td>H</td>
<td>Phenyl</td>
<td>Hexa-H-Phenyl-Br-F</td>
<td>61</td>
</tr>
<tr>
<td>185</td>
<td>OTBDMS</td>
<td>Phenyl</td>
<td>Hexa-OTBDMS-Phenyl-Br-F</td>
<td>73</td>
</tr>
<tr>
<td>186</td>
<td>OH</td>
<td>Phenyl</td>
<td>Hexa-OH-Phenyl-Br-F</td>
<td>83</td>
</tr>
<tr>
<td>187</td>
<td>H</td>
<td>4-Fluorophenyl</td>
<td>Hexa-H-(4-Fluorophenyl)-Br-F</td>
<td>69</td>
</tr>
<tr>
<td>188</td>
<td>OH</td>
<td>4-Fluorophenyl</td>
<td>Hexa-OH-(4-Fluorophenyl)-Br-F</td>
<td>80</td>
</tr>
<tr>
<td>189</td>
<td>H</td>
<td>2-Fluorophenyl</td>
<td>Hexa-H-(2-Fluorophenyl)-Br-F</td>
<td>64</td>
</tr>
<tr>
<td>190</td>
<td>OH</td>
<td>2-Fluorophenyl</td>
<td>Hexa-OH-(2-Fluorophenyl)-Br-F</td>
<td>87</td>
</tr>
</tbody>
</table>

*This dendrimer was obtained via TBDMS deprotection of its TBDMS-protected precursor (185).*

Purification of these dendrimers was performed by preparative TLC, because it was
difficult to remove the traces of unreacted monoadducts and other impurities by using
flash column chromatography. Fluorine-containing dendrimers 187-190 were mostly
purified through reverse-phase HPLC to ensure the purity of the products, because any
impurities that originated from the degradation of F-CPD also possessed aromatic
fluorines and therefore may give rise to unwanted and/or misleading peaks in the 19F
NMR spectra.

Similar to the unsymmetrical pentaaryl dendrimers, the 13C NMR spectra of the
unsymmetrical hexaaryl dendrimers showed that each carbon appeared at the same
chemical shift as their symmetrical analogues. The 1H NMR spectra of the parent
unsymmetrical dendrimers showed that the AB pattern that was observed in the parent
analogue had doubled and merged. The information that could be obtained from the 1H
and 13C NMR spectra of these dendrimers was limited and as previously, the structural
proof was obtained mainly from MALDI-TOF (Appendix A).
As with $^{13}$C NMR, peak duplication was also observable in the $^{19}$F NMR spectra of fluorine-containing dendrimers. Figure 2-41 shows the $^{19}$F NMR spectra comparison of 187 with its symmetrical analogues 168 and 169. This assignment was also supported by 2D NMR measurements that are described in detail in Chapter 3. This method of assignment was also used during the $^{19}$F peak identification of the compounds obtained by derivatising these dendrimers.

![Figure 2-41 $^{19}$F NMR spectra (470 MHz) comparison of dendrimers 169 (top), 187 (middle) and 168 (bottom). (▲ = $^{19}$F peaks from Br side; ▲ = $^{19}$F peaks from F side; ● = peripheral $^{19}$F)](image)

Unfortunately in ortho-substituted unsymmetrical dendrimer 189, it was difficult to assign each $^{19}$F peak to its respective sides because they appear very close to each other. Additionally, an unexpected peak splitting was observed in the first set of peaks in the $^{19}$F NMR spectrum of this dendrimer. The comparison of the spectra of this dendrimer with its symmetrical analogues (dendrimers 171 and 172) reveals peak ambiguity (Figure 2-42).

In Figure 2-42 (a) it was observed that the number of $^{19}$F peaks in unsymmetrical dendrimer 189 had doubled. Enlargement of the first two peaks in this dendrimer (Figure 2-42 (b)) revealed that they had formed what looked like a quartet. The peripheral $^{19}$F peaks (Figure 2-42 (c)) of both 172 and 187 possessed similar patterning, indicating that the peripheral fluorines experienced similar chemical environment in
both symmetrical and unsymmetrical dendrimers. Similar quartet-like splitting pattern was also observed in the analogue dendrimer Hexa-OH-(2-Fluorophenyl)-Br-F (190).

\[\text{Symmetrical Hexa-H-(2-Fluorophenyl)-F-F} \]
(172)

\[\text{Unsymmetrical Hexa-H-(2-Fluorophenyl)-Br-F} \]
(189)

\[\text{Symmetrical Hexa-H-(2-Fluorophenyl)-Br-Br} \]
(171)

\[\text{Symmetrical Hexa-H-(2-Fluorophenyl)-F-F} \]
(172)

\[\text{Unsymmetrical Hexa-H-(2-Fluorophenyl)-Br-F} \]
(189)

Figure 2-42 $^{19}$F NMR spectra (470 MHz) comparison of dendrimers 172 (top), 189 (middle) and 171 (bottom) for the central fluorine. (a) Overall spectra showing only central fluorine peaks, it is evident that the $^{19}$F peaks have doubled; (b) Enlargement of the first set of central $^{19}$F peaks in the same order; ▲ and ▼ show that the first two $^{19}$F peaks of dendrimer 189 do not only double but also split and form what looks like a quartet; (c) Comparison of the peripheral $^{19}$F peaks of dendrimers 172 (top) and 189 (bottom) showing the peripheral fluorines on both dendrimers give rise to similar pattern in $^{19}$F NMR, albeit slightly different in chemical shifts.
The lineshape profile of this peak is similar to that of the AB quartet at about 6.15 ppm previously observed in $^{1}\text{H}$ NMR of parent-type dendrimers. In order to establish whether or not the observed quartet is an AB quartet, variable temperature (VT) $^{19}\text{F}$ NMR of 189 was performed. The temperature was varied from 263 K to 323 K, in 10 K increments. The resulting spectrum for each temperature was then enhanced with Lorentz-to-Gauss transformation to obtain better resolution so that the splitting could be better observed (Figure 2-43).

![Figure 2-43](image)

*Figure 2-43* VT $^{19}\text{F}$ NMR result (470 MHz) of unsymmetrical dendrimer 189, focusing only on the first set of peaks. Full results are available in Appendix C. Red: peaks with Lorentzian lineshape. Blue: the same peaks with Gaussian lineshape obtained through Lorentz-to-Gauss transformation. Bottom right spectrum shows the peak profile at room temperature (298 K) annotated with AB coupling constant (see main text).

If the peak was a quartet, the intensity ratio and the distance between each line would remain the same at all temperatures, but VT NMR revealed otherwise. This suggests that the splitting was caused by coupling of the $^{19}\text{F}$ nuclei to other NMR-active nuclei. The only nuclei that were present in this dendrimer were $^{1}\text{H}$, $^{13}\text{C}$ and $^{19}\text{F}$. Owing to the natural abundance of $^{13}\text{C}$ nuclei, $^{19}\text{F}$ peaks coupled to $^{13}\text{C}$ nuclei will always appear as satellites. There would be no $^{19}\text{F}$ peaks that coupled to $^{1}\text{H}$ nuclei since $^{1}\text{H}$-decoupling was performed. Therefore, the splitting could only be caused by a coupling to another $^{19}\text{F}$ nucleus (homonuclear $^{19}\text{F}–^{19}\text{F}$ coupling). Moreover, considering that the fluorines in this dendrimer are separated by 12 bonds, the homonuclear $^{19}\text{F}–^{19}\text{F}$ coupling could not have resulted from through-bond coupling but rather from through-space coupling.
Through-space coupling has long been known and usually observed between nuclei such as $^{19}$F with itself or with other NMR-active nuclei such as $^1$H, $^{13}$C, $^{14}$N, $^{31}$P or $^{77}$Se. This coupling is known to have arisen from nonbonded interactions between two nuclei separated by four or more bonds but are spatially in close proximity. One convincing piece of evidence for the through-space coupling phenomena was reported in 1978 by Feeney and co-workers who studied a dihydrofolate reductase enzyme that contained $^{19}$F-labelled tryptophan residues. They observed through-space coupling between two $^{19}$F nuclei (through-space coupling constant, $T^S_{F-F} = 17$ Hz) that were separated by 127 amino acid residues (398 bonds) but were spatially in close proximity. In 2000, the observation was confirmed by Oldfield and co-workers who performed computational modelling of the enzyme and found that the distance between the two $^{19}$F nuclei ($d_{F-F}$) was 2.98 Å.

In a theory proposed by Mallory using $^{19}$F–$^{19}$F as a model, the nonbonded interaction is suggested to be caused by the overlap of the orbitals of the two $^{19}$F nuclei due to close proximity. The overlap converts the pair of $p$ orbitals into a two-center molecular orbital: a weakly bonding and a weakly antibonding orbitals (Figure 2-44). Since each of the $p$ orbitals contain lone-pair electrons, both the bonding and antibonding orbitals of the newly formed molecular orbitals are filled. Mallory argued that even though this does not lead to chemical bonding, it provides a linkage between the two nuclei, enabling the transmission of nuclear spin information between them and therefore giving rise to through-space coupling.

![Figure 2-44](image-url) Overlap of two $^{19}$F nuclei orbitals forming a molecular orbital. The orbitals $p_{F\sigma}$ and $p'_{F\sigma}$ refer to the first and the second $^{19}$F nuclei involved in the coupling.

It is known that the magnitude of the coupling constant is distance-dependent because through-space coupling only arises when the two nuclei are in close proximity. Efforts have been directed towards establishing the relationship between the two variables through experimental and computational modelling. The group of Mallory and Ernst have independently investigated this using two families of compounds with different
rigidity (Figure 2-45).

Mallory and co-workers used various difluoronaphthalenes derived from 191 and 192 in their studies. On the other hand, Ernst and Ibrom used various difluorocyclophanes (196-200 and some of their derivatives) which are more flexible than the naphthalenes and are able to rotate, resulting in larger $d_{F-F}$ ($198$ and $200$). Despite the difference in structural flexibility, both groups agreed that the coupling constant decays rapidly as the distance increases (Figure 2-46) and established two slightly different expressions.

In this thesis, the expression proposed by Ernst and Ibrom was used because it was deemed more appropriate since the flexibility of the cyclophanes are better than the naphthalenes in representing the dendrimers. The expression is shown in Eq. (1):\textsuperscript{118}
\[ TSJ_{F,F} = (2.75 \times 10^5) e^{-3.211d_{F,F}} \]  

Eq. (1)

where \( TSJ_{F,F} \) is the through-space coupling constant (Hz) and \( d_{F,F} \) is the distance between the two \(^{19}\text{F} \) nuclei (Å) involved in the coupling. Because the coupling constant value is obtained experimentally in this research, the equation is rewritten to solve \( d_{F,F} \) for \( TSJ_{F,F} \), as expressed in Eq. (2).

\[
d_{F,F} = \frac{\ln (2.75 \times 10^5) - \ln TSJ_{F,F}}{3.211}
\]

Eq. (2)

The through-space coupling was observed not only in dendrimer 189 but also in its OH-containing analogue 190, giving a similar splitting pattern. From the VT \(^{19}\text{F} \) NMR spectra and the value of \( \Delta\nu/J \) of the peaks in both dendrimers (1.8 and 2.3 for 189 and 190 respectively) the peak splitting caused by the through-space coupling was established as an AB-type splitting.

Table 2-15 summarises the information obtained after resolving the AB pattern of both \( \text{ortho} \)-substituted unsymmetrical dendrimers. The Lorentz-to-Gauss transformation enhancement was used to obtain more accurate chemical shifts and coupling constants.

<table>
<thead>
<tr>
<th>Dendrimer 189</th>
<th>Dendrimer 190</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexa-H-(2-Fluorophenyl)-Br-F</td>
<td>Hexa-OH-(2-Fluorophenyl)-Br-F</td>
</tr>
<tr>
<td>( J_{AB}^a )</td>
<td>470 MHz</td>
</tr>
<tr>
<td>( J_{AB}^b )</td>
<td>3.7 Hz</td>
</tr>
<tr>
<td>( \Delta\nu_{AB} )</td>
<td>6.67 Hz</td>
</tr>
<tr>
<td>( d_{F,F}^c )</td>
<td>3.49 Å</td>
</tr>
</tbody>
</table>

\( ^a \) Peaks 1 and 2 of unsymmetrical dendrimers 189 and 190 also enhanced with Lorentz-to-Gauss transformation (blue).

\( ^b \) AB coupling constant \( (J_{AB}) \) is also through-space coupling constant \( (TSJ_{F,F}) \).

\( ^c \) \(^{19}\text{F}–^{19}\text{F} \) distance calculated from Eq. (2).

Table 2-15 Information obtained from the AB pattern in dendrimers 189 and 190.

The distance between the two \(^{19}\text{F} \) nuclei involved in the through-space coupling was calculated using Eq. (2) from the known \( TSJ_{F,F} \) value. As a comparison, the shortest \(^{19}\text{F}–^{19}\text{F} \) distance...
\(^{19}\)F distance in dendrimer 189 was calculated through DFT calculation at the M06-2X/6-31G** and wB97xD/6-31G** level of theory (Table 2-16). The symmetrical analogue (171) was also calculated with the same level of theory and compared with the results obtained for unsymmetrical dendrimer 189.

<table>
<thead>
<tr>
<th>Dendrimer</th>
<th>Level of Theory</th>
<th>(d_{FF}) (Å)</th>
<th>(\alpha)</th>
<th>(\beta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>189</td>
<td>M06-2X/6-31G**</td>
<td>3.91</td>
<td>125.4</td>
<td>128.4</td>
</tr>
<tr>
<td></td>
<td>wB97xD/6-31G**</td>
<td>3.27</td>
<td>130.1</td>
<td>130.3</td>
</tr>
<tr>
<td>171</td>
<td>M06-2X/6-31G**</td>
<td>3.60</td>
<td>130.3</td>
<td>130.3</td>
</tr>
<tr>
<td></td>
<td>wB97xD/6-31G**</td>
<td>3.41</td>
<td>133.5</td>
<td>133.5</td>
</tr>
</tbody>
</table>

Table 2-16 DFT calculation result for conformers with fluorines in close proximity. The wB97xD functional takes into account long-range correlation. The angle of C–F···F is expressed as \(\alpha\) when measured from the Br-side and \(\beta\) when measured from the F-side. In symmetrical dendrimer 171, \(\alpha = \beta\).

As modelled through computational calculation, the conformer with the closest central fluorines in dendrimer 189 and 171 is shown Figure 2-47. This conformer possesses \(C_2\) symmetry in dendrimer 171 but not in 189.

![Figure 2-47](image)

**Figure 2-47** The dendrimer conformation that possesses fluorines in close proximity. (a) Unsymmetrical dendrimer 189; (b) Symmetrical dendrimer 171.

Although the through-space coupling is clearly observable on the unsymmetrical dendrimers 189 and 190, it is not observed in their symmetrical analogues (dendrimers 171, 172 and 173) as previously shown in \(^{19}\)F NMR comparison in Figure 2-42 (a). In the symmetrical analogue, both fluorines are magnetically equivalent and therefore, although these symmetrical dendrimers may form conformers in which the central

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\(^{iii}\) All computational calculations in this thesis were performed by Dr Mark Vincent, Senior Experimental Officer, The University of Manchester, using Gaussian09 software.
fluorines are in close proximity, through-space coupling would not be observed. Breaking the symmetry and forming unsymmetrical dendrimers causes magnetic inequivalency and through-space coupling becomes observable.

In conclusion, a series of pentaaryl and hexaaryl dendrimers have been synthesised. Stereoisomerism was indicated either in the X-ray crystallography results or through the $^{19}$F NMR spectra. Conformational studies of these dendrimers were carried out to fully understand this behaviour and are described in detail in the next chapter.
3 Atropisomerism, Resolution Attempt and Energetics of Dendrimers

3.1 Introduction to Atropisomerism

Organic compounds may exist as stereoisomers when there is restricted rotation around a bond (axis), and such stereoisomers are known as atropisomers. The term ‘atropisomer’, first coined by Kuhn in 1933, is derived from Greek α (not) and τροπός (turn). Also known as axial chirality, atropisomerism is observed when there are steric or electronic constraints, resulting in a high energy barrier that restricts the free rotation of the axis. This consequently gives rise to the formation of conformational isomers leading to diastereomers or enantiomers. If the interconversion is slow enough, individual isomers can be observed, and in some cases, isolated. These conformational isomers, possess the distinctive feature that enables them to be thermally equilibrated and to give rise to epimerisation or racemisation. Compounds with chiral centers are usually stable and can only racemise via a bond breaking and forming process. On the contrary, atropisomers are less stable since they are capable of racemisation simply via a bond rotation. Depending on the degree of conformational constraint, temperature or solvent, the half-lives of atropisomer racemisations may vary from the order of seconds to years. By definition, the half-life of atropisomer should be longer than 1000 seconds at any given temperature so that they can be observed and isolated. This corresponds to a free energy of activation (ΔG°‡) of more than approximately 22.3 kcal mol⁻¹ or 93.3 kJ mol⁻¹ at room temperature (300 K). Compounds with half-lives shorter than 1000 seconds (and therefore ΔG°‡ of less than the aforementioned values), are considered to have fast interconversion. These types of compounds are known as tropos or ‘near-atropisomer’. Figure 3-1 shows several compounds that exhibit atropisomerism. The first isolated atropisomer was 6,6’-dinitrodiphenic acid (201), reported almost a century ago by Christie and Kenner, that was isolated through fractional crystallisation. Atropisomers also exist in naturally occurring compounds such as vancomycin (202), an antibiotic isolated from Amycolatopsis orientalis, and Myristinin B (203), a selective cyclooxygenase (COX-2) enzyme inhibitor and antifungal agent isolated from Myristica cinnamomea. Atropisomers have also been used as ligands to catalyse...
various reactions such as asymmetric homo-coupling of 2-naphthols \((204)^{130}\) and enantioselective allylation of aldehydes \((205)^{131}\). Drugs containing atropisomers have also been produced such as Telenzepine \((206)\) and Sch 40120 \((207)\).\(^{123,124}\)

\[ \text{Figure 3-1} \] Examples of compounds that exhibit atropisomerism. Chiral axes are shown as bold red axes. (a) The first isolated atropisomer; (b) Natural products that contain atropisomers; (c) Compounds with atropisomers used as catalysts and; (d) as drugs.\(^ {122–124,127,129–131}\)

Telenzepine \((206)\) shows that atropisomerism may arise not only from two rings directly connected to each other, but also from fused ring system. In fact, since the existence of atropisomers stems from the restriction of bond rotation, any compounds with enough steric constraint to restrict intramolecular rotation may exhibit atropisomerism. Clayden and co-workers have excellently demonstrated this through a series of benzamide derivatives \((208-218)\). Figure 3-2 that exhibit atropisomerism with increasing order of half-lives from seconds to years as steric constraint increases.

\[ \text{Figure 3-2} \] Several benzamide derivatives that exhibit atropisomerism along with their estimated racemisation half-lives and bond rotation energy barrier at 25 °C. Chiral axes are shown as red axes. Adapted from Clayden.\(^ {126}\)
The stereochemical configuration of atropisomers is determined by analysis of the Newman projection of the corresponding compound as exemplified in Figure 3-3. After the priorities of the substituents have been assigned according to the Cahn-Ingold-Prelog rules, the shortest 90° turn from 1 (substituent with highest priority on the proximal ring) to 1' (substituent with highest priority on the distal ring) is analysed. If the turn is clockwise, the atropisomer is assigned as $P$ (for plus); and if it is counterclockwise, the atropisomer is assigned as $M$ (for minus).\textsuperscript{122}

![Configuration assignment of compound 201.](image)

**Figure 3-3** Configuration assignment of compound 201.

### 3.2 Measuring the Kinetic Parameters of Atropisomers

One of the most useful techniques used to recognise the existence of atropisomers is NMR spectroscopy. The advantage of NMR is its capability to detect chemical exchange; even if the exchange is in equilibrium at the macroscopic level, an individual nucleus experiences a change in chemical environment at the microscopic level. There may not be any observable changes in the sample but a chemical process has occurred from the standpoint of a particular nucleus and therefore NMR is able to easily detect this.\textsuperscript{132} NMR has been used to study the dynamics of various species from small molecules such as dimethylacetamide\textsuperscript{132} and organometallic complexes\textsuperscript{133,134} to large molecules such as proteins\textsuperscript{135} and supramolecular complexes.\textsuperscript{136}

![Conformational equilibrium giving rise to chemical exchange.](image)

**Figure 3-4** Conformational equilibrium giving rise to chemical exchange.

Chemical exchange may arise from two different equilibria: conformational equilibrium (Figure 3-4) and chemical equilibrium (e.g. exchange of OH proton with other protons in a solution).\textsuperscript{137,138} Racemisation or epimerisation of atropisomers that gives rise to
Axial Chirality and Conformational Studies

chemical exchange stems from the conformational equilibrium between the isomers, which is an intramolecular process. Because an intramolecular process is a unimolecular process, the interconversion of atropisomers follows first-order kinetics. In the study of chemical exchange that results in atropisomerism, the rates of conformer interconversion and the half-lives of each conformer are two of the most important aspects to investigate.

Chemical exchange can be studied via 1D Variable Temperature (VT) dynamic NMR (DNMR) or 2D Exchange Spectroscopy (EXSY) NMR measurements. In VT DNMR, the information on the rate constants that govern the exchange are contained within the peak lineshapes of the exchanging nuclei. As temperature increases, rate constants increase, causing the line of these peaks to broaden, coalesce and sharpen again. Two widely used methods to determine the rate constants from VT DNMR are the ‘coalescence method’ and the ‘complete lineshape analysis’ (CLSA). The former is only capable of determination of rate constants at the coalescence temperature. For a two-site system comprised of uncoupled nuclei with equal populations, this can be expressed in Eq. (3).

\[ k_{\text{coalescence}} = \frac{\pi \Delta \nu}{\sqrt{2}} \]  

where \( k_{\text{coalescence}} \) is the rate constant at coalescence temperature and \( \Delta \nu \) is the frequency difference (Hz) between the peaks in the absence of exchange. The most accurate method to extract rate constants from VT NMR measurements is the CLSA method, whereby the obtained experimental lineshapes are simulated computationally using various kinetic and spectroscopic parameters until the best fit is obtained.

When a system undergoes slow exchange, the exchange rate is not fast enough to significantly affect the line broadening in the 1D NMR spectrum. Therefore, the estimation of rate constant by relying on the 1D NMR lineshape is discouraged since it is difficult to differentiate the line broadening that stems from chemical exchange from other line-broadening factors such as magnetic field inhomogenities. For this reason, 2D EXSY is used to study systems with slow exchange. The 2D EXSY measurement is capable of detecting slow exchange among multiple exchange sites and therefore enables the mapping of complex exchange networks.
One of the most important parameters in 2D EXSY is the mixing time \( (t_m) \), during which chemical exchange occurs.\(^{139} \) In this period, the magnetisation is transferred from one spin to another spin it is exchanging with, resulting in a cross peak in the 2D spectrum. Optimal mixing time should be selected when running an EXSY experiment because if the mixing time is too short, the intensity of the cross peaks will be weak, making cross peaks observation and accurate kinetic measurement difficult. Conversely, if the mixing time is too long, the intensity of the cross peaks will decrease owing to the spin-lattice (\( T_1 \)) relaxation, consequently making cross peaks observation difficult (Figure 3-5 (a)).\(^{136,140} \)

The cross peaks in an EXSY spectrum display the connection of the sites (nuclei) that are exchanging between each other (e.g. A ⇌ B exchange in Figure 3-5). The rate constant of each pair of exchanging nuclei can be estimated by comparing the intensities of the diagonal peaks with the cross peaks.\(^{139} \) The intensities of these peaks obey the equations expressed in Eq. (4), (5) and (6):\(^{139,141} \)
where $I_{AA}$ and $I_{BB}$ are the intensities of diagonal peaks, $I_{AB}$ and $I_{BA}$ are the intensities of cross peaks, $X_A$ and $X_B$ are the mole fractions of A and B respectively, $t_m$ is the mixing time, $R_1$ is the spin-lattice relaxation rate ($T_1^{-1}$), $k$ is the exchange rate constant and $M^0$ is the magnetisation vector. If these equations were plotted ($I$ vs. $t_m$), the result would be the graph shown in Figure 3-5 (b). Additionally, the sum of both mole fractions equals to one as expressed in Eq. (7).

$$X_A + X_B = 1$$  \hspace{1cm} \text{Eq. (7)}

Combination of Eq. (4), (5) and (6) solving for $k$ results in Eq. (8):\(^{139}\)

$$k = \frac{1}{t_m} \ln \frac{r + 1}{r - 1}$$  \hspace{1cm} \text{Eq. (8)}

where $r$ is the ratio of the sum of diagonal and cross peaks intensities. This equation enables the determination of total rate constant from experiments at a single mixing time and is independent of spin-lattice relaxation rate.\(^{141}\)

For an exchange system with equal populations (i.e. $X_A = X_B$), the ratio is defined as the comparison of the sums of the diagonal peak intensities with the sum of the cross peak intensities.\(^{139}\) For an exchange system with unequal populations (i.e. $X_A \neq X_B$), the population in each system has to be taken into account to obtain the ratio, as expressed in Eq. (9):\(^{139}\)

$$r = \frac{4 (X_A X_B) (I_{AA} + I_{BB})}{(I_{AB} + I_{BA})} = (X_A - X_B)^2$$  \hspace{1cm} \text{Eq. (9)}

This equation also works for an exchange system with equal populations because the mole fractions of such a system do not affect the ratio. In this type of system, $4 (X_A X_B)$ would equal to one while $(X_A - X_B)^2$ would be equal to zero.
Although time consuming, more accurate rate constants can be obtained by running the EXSY experiments with a series of varying mixing times. The intensities of the cross peaks and diagonal peaks obtained from the experiments are then plotted ($I$ vs. $t_m$) and fitted to Eq. (4), (5) and (6) to simultaneously extract the rate constants and the other variables. The fitting process in this thesis was performed using Mathematica software, distributed by Wolfram Research Inc. For other experiments with only a single mixing time, the rate constants were extracted using Eq.(8) and (9).

Fitting of $I$ vs. $t_m$ using Eq. (4), (5) and (6) (experiments with varying $t_m$) or calculation using Eq. (8) (experiments with single $t_m$) yields the total rate constant of a two-site exchange system. The relationship between the total rate constant with the individual rate constants (i.e. the rate constants of the forward and reverse processes) for the determination of the individual rate constants are expressed by:

$$k = k_f + k_r$$  \hspace{1cm} \text{Eq. (10)}

$$k_f X_A = k_r X_B$$  \hspace{1cm} \text{Eq. (11)}

$$k_f = X_B k$$  \hspace{1cm} \text{Eq. (12)}

$$k_r = X_A k$$  \hspace{1cm} \text{Eq. (13)}

where $k_f$ is the rate constant of the forward process ($k_{AB}$ in Figure 3-5) and $k_r$ is the rate constant of the reverse process ($k_{BA}$ in Figure 3-5).

In this research, most of the exchange networks obtained were four-site exchange instead of two-site exchange. The determination of rate constants for these systems was difficult and therefore was performed by the two-site approach, whereby the four-site system was broken into four sets of two-site systems (Figure 3-6).

**Figure 3-6** Treatment of four-site exchange in this research. (a) Typical four-site exchange network observed in this research; (b) Broken down into four sets of two-site exchange. Determination of the rate constants of each system was performed using short mixing times and in the same way as a true two-site exchange.

The determination of rate constants of the four-site exchange system using this approach was performed at shorter mixing times. At longer mixing times the long-range indirect
exchange cross peaks (i.e. A ⇄ D or B ⇄ C) were observed as a result of sequential exchange (i.e. A ⇄ B (or C) ⇄ D or B ⇄ A (or D) ⇄ C), rendering the two-site approach incorrect and reducing the accuracy of rate constant determination.

An alternative method for the determination of the four-site exchange rate constants is by using EXSYCalc software, distributed by Mestrelab Research. The advantage of using this program is that it directly calculates the individual rate constants instead of the total rate constants. The disadvantage is that it can only solve the rate constants from experiments with a single mixing time. In this research, the rate constants of the four-site exchange obtained from the two-site approach were compared to those obtained from the software. The software is also capable of solving the rate constants of two-site exchange system; however, due to the disadvantage mentioned above, the rate constants determination for this system was performed by fitting to Eq. (4), (5) and (6) instead.

Several publications recommend avoiding experiments with varying mixing times, even though they improve the precision of rate constant measurement, because they are time consuming and may cause systematic errors due to long-term instrument instabilities. Other publications recommend these experiments, emphasising the importance of accurate rate constants. In this research, mixing time experiments were performed only for the dendrimers that were modelled computationally and their derivatives with chiral auxiliary attached. The rate constants of other dendrimers were obtained from experiments with a single mixing time.

3.3 Measuring the Thermodynamic Parameters of Atropisomers

Interconversion of atropisomers requires rotation about the chiral axis until a certain energy barrier is passed, followed by continued rotation to form the other stable atropisomer. The measurement of the rate constant of interconversion from both 1D and 2D NMR spectra allows for the calculation of the experimental energy barrier and other thermodynamic parameters using the Arrhenius and Eyring equations. The temperature dependence of reaction rate is described by the Arrhenius equation:

$$k = A e^{\left(\frac{-E_a}{RT}\right)}$$

$$\ln k = -\frac{E_a}{R} \left(\frac{1}{T}\right) + \ln A$$
where \( k \) is the rate constant, \( A \) is the pre-exponential factor, \( E_a \) is the activation energy, \( R \) is the gas constant (8.3144 J K^{-1} mol^{-1}) and \( T \) is the temperature. The rewritten expression (Eq. (15)) can be used to make a plot of \( \ln k \) vs. \( (1/T) \), to determine the values of \( E_a \) and \( A \). These values can only be obtained when the rate constants at various temperatures are known.

The activation energy is defined as the minimum kinetic energy that must be possessed by the reactants to form the products. The pre-exponential factor measures the rate at which collisions take place irrespective of their energy. The product of the pre-exponential factor and the exponential factor \((-E_a/RT)\) gives the rate constant which can also be translated as the successful collisions that yield products.\(^{137}\)

![Figure 3-7](image)

**Figure 3-7** Potential energy surface of a reaction. (a) Defined in terms of \( E_a \) and \( \Delta H \); (b) Defined in terms of \( \Delta G^\circ \) and \( \Delta G \).

Figure 3-7 shows the potential energy surface of a reaction. The difference in energy between the starting material and the transition state (TS) is the activation energy, whilst the difference in energy between the starting material and the product is the enthalpy of reaction (\( \Delta H \)). In terms of Gibbs free energy (Figure 3-7 (b)), the difference in energy between the starting material and TS is the \( \Delta G^\circ \), whilst the difference in energy between the starting material and the product is the Gibbs free energy of reaction (\( \Delta G \)).

The Eyring equation expresses the relationship of rate constant with the Gibbs free energy of activation (\( \Delta G^\circ \)).\(^{138}\)

\[
k = \kappa \frac{k_BT}{h} e^{-\frac{\Delta G^\circ}{RT}} \quad \text{Eq. (16)}
\]

where \( k \) is the rate constant, \( \kappa \) is the transmission coefficient (1), \( k_B \) is the Boltzmann
constant \((1.38 \times 10^{-23} \text{ J K}^{-1})\), \(T\) is the temperature, \(h\) is the Planck constant \((6.626 \times 10^{-34} \text{ J s})\), \(\Delta G^\ddagger\) is the Gibbs free energy of activation and \(R\) is the gas constant. Rewriting the Eyring equation to solve for \(\Delta G^\ddagger\) enables the determination of \(\Delta G^\ddagger\) at temperatures with known rate constants.

\[
\Delta G^\ddagger = -RT \ln \left( \frac{k_B T}{k h} \right) \tag{17}
\]

In cases where the values of rate constant at various temperatures are known, the Eyring equation can also be used to determine the enthalpy of activation (\(\Delta H^\ddagger\)) and the entropy of activation (\(\Delta S^\ddagger\)) by constructing a plot between \(\ln \left( \frac{k}{T} \right)\) vs. \(\frac{1}{T}\) and using the rewritten expression (Eq. (19)).

\[
\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \tag{18}
\]

\[
\ln \left( \frac{k}{T} \right) = -\frac{\Delta H^\ddagger}{R} \frac{1}{T} + \frac{\Delta S^\ddagger}{R} + \ln \left( \frac{k_B}{h} \right) \tag{19}
\]

NMR experiments are typically performed at a narrow range of temperatures due to solvent limitation. Consequently, only a narrow range of rate constants can be obtained. Therefore, the values of \(\Delta H^\ddagger\) and \(\Delta S^\ddagger\) obtained from the Eyring plot usually have a large margin of error, but nevertheless, are still able to depict the energy profile of a process. Furthermore, it has also been said that the determination of \(\Delta S^\ddagger\) using the Eyring plot is unreliable because it is obtained via extrapolation to infinite temperature. Lente and co-workers have shown that this is not the case and argued that the margin of error of \(\Delta S^\ddagger\) obtained from the Eyring plot does not stem from extrapolation to infinite temperature, but rather because of the narrow range of temperatures at which the experiments are performed.

### 3.4 Atropisomerism of the Synthesised Polyarene Dendrimers

In the pentaaryl dendrimers, evidence of atropisomerism presence was not observed spectroscopically despite the existence of chiral axes. X-ray crystallography of several pentaaryl dendrimers (Figure 2-8, Figure 2-9 and Figure 2-14 in Chapter 2) showed that in the solid state they crystallise in various atropisomeric conformations. The low steric constraints evidently result in fast atropisomer interconversion in solution at ambient temperature, consequently making separation of atropisomers not feasible.
Various NMR spectra (\(^1\)H, \(^{13}\)C and \(^{19}\)F NMR) of the hexaaryl dendrimers, previously discussed in Section 2.7 in Chapter 2, evidenced atropisomerism. The fact that the physical separation of these dendrimer atropisomers was not achieved most likely stems from the moderate interconversion rates, slow enough to enable spectroscopic observations but not slow enough to enable physical separation due to racemisation and/or epimerisation during isolation timescales.

In Sections 3.6, 3.7 and 3.8, attempts to investigate these observations were undertaken through various NMR spectroscopic studies, which revealed how the atropisomers undergo interconversion. Quantitative analysis of the NMR spectra revealed the values of interconversion rate constant and their respective energy barriers, which ultimately provide insight into how the dendrimer atropisomers interconvert. The dendrimers were also subjected to reactions with chiral auxiliaries to enable spectroscopic observation of diastereomers and to slow down the atropisomer interconversion in an attempt to physically separate the atropisomers.

### 3.5 Axial Chirality of Symmetrical and Unsymmetrical Pentaaryl Dendrimers

The pentaaryl dendrimers are sterically less crowded than the hexaaryl dendrimers, as they have two aromatic rings fewer. Nevertheless, there are two chiral axes (dendrimer arms) in pentaaryl dendrimers that connect the left and right moieties to the central core. Both of the dendrimer arms are chiral because each of them connects two aromatic rings with different substituents.

The pentaaryl dendrimers should, in theory, exist as four atropisomers due to the presence of two chiral axes in the structure (Figure 3-8). This is true for the unsymmetrical dendrimers; but for the symmetrical dendrimers, two of the enantiomers (atropoenantiomers) exist as a pair of meso compounds.

![Figure 3-8](image-url) Four possible conformations in pentaaryl dendrimer in general.
Additionally, both conformers represented by the dashed red line in Figure 3-8. On the other hand, conformers \( \text{a} \) and \( \text{b} \) possess a plane of symmetry that can also be represented by the dashed red line in Figure 3-8. On the other hand, conformers \( \text{c} \) and \( \text{d} \) would remain unchanged if they were rotated \( 180^\circ \) and therefore they are two conformers with \( C_2 \) symmetry with axes of symmetry shown as dashed red lines.

Using the conformers in Figure 3-8 as a reference, the symmetrical pentaaryl dendrimer Penta-OH-Br-Br (153), with all the possible conformations it exists in, their respective stereochemical configuration and the relationship among each conformer are shown in Figure 3-9. This illustration is a representative for all symmetrical pentaaryl dendrimers described herein.

**Figure 3-9** Penta-OH-Br-Br (153) in all possible conformations (dendrimer arms shown in blue).

Evidence of these atropisomers can be seen in the solid state from the X-ray crystallography results of pentaaryl dendrimers 153 and 154. The X-ray crystallography results of both dendrimer have been shown previously in Figure 2-8 and Figure 2-9 in Chapter 2. Dendrimer 153 crystallises as a pair of meso compounds while dendrimer 154 crystallises as a pair of enantiomeric conformers with \( C_2 \) symmetry. The stereochemical assignment of these conformations is shown in Figure 3-10 and Figure 3-11.
Axial Chirality and Conformational Studies

Figure 3-10 ORTEP drawing of dendrimer 153, showing that it crystallises as the achiral meso compounds: \((P, M)\) and \((M, P)\).

Figure 3-11 ORTEP drawing of dendrimer 154, showing that it crystallises as the pair of enantiomers: \((M, M)\) and \((P, P)\).
Axial Chirality and Conformational Studies

In the unsymmetrical dendrimers, the same conformers are still present however there is a slightly different atropisomeric system. Breaking the symmetry eliminates the existence of meso compounds as well as the $C_2$ symmetry previously present in the symmetrical dendrimers. Therefore, the unsymmetrical pentaaryl dendrimers can exist as four conformers, which consist of two sets of diastereomers, each of which consists of a pair of enantiomers (Figure 3-12).

![Figure 3-12](image)

Figure 3-12 Penta-H-Br-F (dendrimer 157) in all possible conformations with dendrimer arms shown in blue.

In the solid state, dendrimer 157 crystallises as the $(P, P)$ and $(M, M)$ conformers (Figure 3-13). Similar to the symmetrical dendrimer 154, the $(P, M)$ and $(M, P)$ conformers of this dendrimer were not observed in the X-ray data.

Even though X-ray crystallography results showed the presence of atropisomers in the solid state, the NMR spectra of all of the pentaaryl dendrimers did not show indication of atropisomer presence, suggesting that interconversion occurs very fast at room temperature. In order to observe the presence of atropisomers, the interconversion has to be slowed. This can be achieved by performing the NMR experiments at lower temperatures or by introducing additional steric hindrance to the focal moiety of the dendrimer. The latter option was chosen because it was judged to be more practicable than the former.
3.6 Chiral Resolution Attempts of Pentaaryl Dendrimers

It has been shown that both symmetrical and unsymmetrical pentaaryl dendrimers exist as atropisomeric conformers in the solid state, but in solution, fast interconversion from dendrimer arm rotations prevents their spectroscopic observation. In an attempt to slow down the rotation, additional steric hindrance in the form of a chiral auxiliary was introduced to the focal moiety of pentaaryl dendrimer. A chiral auxiliary was chosen to hamper the arms rotation and to simultaneously convert the pairs of enantiomers into diastereomers to enable observation via NMR spectroscopy and potentially allow physical separation of atropisomers (resolution) via chromatographic techniques.

The chiral auxiliaries employed were amino acid auxiliary (S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl butanoic acid (219) and camphor auxiliary (+)-(1S)-10-camphorsulphonic chloride (220) as shown in Figure 3-14. An analogue of the amino acid auxiliary (R-α-methyl instead of S-α-isopropyl) has been used in enantiomeric resolution of helicenes by Moussa and co-workers. Therefore, it was anticipated that by making the α substituent bulkier (isopropyl), compound 219 would add crowdedness, slow the dendrimer arm rotations and therefore enable atropisomer resolution.
Esterifications of the dendrimers with 219 were carried out under the Steglich esterification conditions (DCC, DMAP and CH$_2$Cl$_2$ at room temperature). These conditions were employed because Neises and Steglich reported that this method was very efficient and that sterically demanding esters could be obtained in good yields at room temperature.$^{145}$ Esterifications of the dendrimers with camphor sulfonyl chloride 220 were performed simply under basic conditions (triethylamine) to promote the formation of sulfonic esters.

Table 3-1 summarises the pentaaryl dendrimers with chiral auxiliaries attached. The amino acid auxiliary is abbreviated as ‘AAux’ whilst the camphor auxiliary is abbreviated as ‘CAux’ in the dendrimer nomenclature.

<table>
<thead>
<tr>
<th>No.</th>
<th>Chiral Agent (R)</th>
<th>Rings D/E (X)</th>
<th>Rings D'/E' (X)</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>221</td>
<td>Amino acid</td>
<td>Br</td>
<td>Br</td>
<td>Penta-OAAux-Br-Br</td>
<td>95</td>
</tr>
<tr>
<td>222</td>
<td>Amino acid</td>
<td>F</td>
<td>F</td>
<td>Penta-OAAux-F-F</td>
<td>72</td>
</tr>
<tr>
<td>223</td>
<td>Amino acid</td>
<td>Br</td>
<td>F</td>
<td>Penta-OAAux-Br-F</td>
<td>92</td>
</tr>
<tr>
<td>224</td>
<td>Camphor</td>
<td>Br</td>
<td>Br</td>
<td>Penta-OCAux-Br-Br</td>
<td>87</td>
</tr>
<tr>
<td>225</td>
<td>Camphor</td>
<td>F</td>
<td>F</td>
<td>Penta-OCAux-F-F</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 3-1 Pentaaryl dendrimers with auxiliaries attached 221-225.

Although the attachment of chiral auxiliaries was successful, physical separation of atropisomers was still not achieved. This suggests that the conformer interconversion of the resulting ester was still too fast for physical separation at room temperature.

In the $^{13}$C NMR spectra of symmetrical esters 221 and 222, two peaks were observed to have split into four peaks (Figure 3-15 (a)-(d)). The $^{13}$C peaks of unsymmetrical dendrimers prior to the attachment of chiral auxiliaries had already split due to lack of
symmetry. Hence, four $^{13}$C peaks in the resulting unsymmetrical ester 223 were observed to have split into eight peaks (Figure 3-15 (e) and (f)).

**Figure 3-15** A portion of $^{13}$C NMR spectra (100 MHz, CDCl$_3$) of esters 221, 222 and 223 along with their respective precursors.

**Figure 3-16** A portion of $^{13}$C NMR spectra (100 MHz, CDCl$_3$) of esters 224 and 225 along with their respective precursors.
Figure 3-16 shows a portion of $^{13}$C NMR spectra of the camphor sulfonate esters 224 and 225. It can be seen that the splitting of the $^{13}$C peaks at approximately 127.5 ppm is not as clear as those with amino acid auxiliary attached (Figure 3-15). This indicates that the camphor auxiliary was not slowing the rotation as much as the amino acid auxiliary. The unsymmetrical dendrimer 158 was not esterified with the camphor auxiliary because based on the results obtained thus far, it was thought that the $^{13}$C NMR profile of the resulting ester would be similar and not very informative.

It was assessed that the dendrimer arm rotations had been slightly slowed by the ester and that at higher temperatures, the $^{13}$C peaks would coalesce into a single peak. To investigate this, VT $^{13}$C NMR study was carried out. The estimated rate constant values as well as the free energy of activation obtained from the VT NMR experiment was expected to give insight into how readily these pentaaryl dendrimers rotate.

![Figure 3-17 A portion of VT $^{13}$C NMR (125 MHz, DMF-$d_7$, 1,4-dioxane) spectra of Penta-OAAux-Br-F (223) from 283 K to 373 K. The set of peaks exhibiting exchage is shown by the black line. Coalescence starts at 313 K and full coalescence occurs at 323 K.](image)

The VT $^{13}$C NMR study was performed on ester 223 as a representative compound (Figure 3-17). Full VT $^{13}$C NMR spectra are available in Appendix C. Due to the low boiling point of deuterochloroform, a more suitable deuterated solvent was needed and
thus deuterated N,N-dimethylformamide (DMF-$d_7$) was chosen. 1,4-Dioxane was also added as an internal standard to act as a chemical shift reference.

CLSA was performed using $dnmr$ module in Bruker TopSpin 3.1 software, to extract kinetic and thermodynamic parameters by relying on the set of peaks at 127.8-128.0 ppm (Table 3-2). It revealed that the interconversion process of the ester occurred rapidly near room temperature (293 K). This consequently meant that the atropisomer interconversion of the parent pentaaryl dendrimers (i.e. those without attached chiral auxiliary) occurred even more rapidly. This explains why the atropisomers could not be observed spectroscopically and why physical separation of both dendrimers and their ester derivatives was not achieved.

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>$k$ (s$^{-1}$)</th>
<th>$\Delta G^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2}$ (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>283</td>
<td>5.43</td>
<td>65.21</td>
<td>127.66</td>
</tr>
<tr>
<td>293</td>
<td>10.13</td>
<td>66.08</td>
<td>68.44</td>
</tr>
<tr>
<td>303</td>
<td>22.04</td>
<td>66.46</td>
<td>31.45</td>
</tr>
<tr>
<td>313</td>
<td>39.60</td>
<td>67.21</td>
<td>17.50</td>
</tr>
<tr>
<td>323</td>
<td>80.70</td>
<td>67.53</td>
<td>8.59</td>
</tr>
<tr>
<td>333</td>
<td>259.76</td>
<td>66.47</td>
<td>2.67</td>
</tr>
<tr>
<td>343</td>
<td>538.74</td>
<td>66.47</td>
<td>1.29</td>
</tr>
<tr>
<td>353</td>
<td>990.12</td>
<td>66.71</td>
<td>0.70</td>
</tr>
<tr>
<td>363</td>
<td>1763.30</td>
<td>66.94</td>
<td>0.39</td>
</tr>
<tr>
<td>373</td>
<td>3648.46</td>
<td>66.61</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Table 3-2 The estimated rate constant values, Gibbs energies of activation and half-lives at each respective temperature for ester 223 obtained via CLSA of the VT $^{13}$C NMR.

The rate constants obtained from various temperatures were used to construct the Arrhenius and Eyring plots. The estimated values for $E_a$, $A$, $\Delta H^0$ and $\Delta S^0$ were 65.27 kJ mol$^{-1}$, $4.25 \times 10^{12}$ s$^{-1}$, 62.57 kJ mol$^{-1}$ and -12.19 J mol$^{-1}$ K$^{-1}$, respectively. The full results (Arrhenius and Eyring plots as well as the resulting simulated spectra at each temperature) are available in Appendix E and F.

Judging from the results obtained from ester 223 as well as the $^{13}$C NMR of the camphor sulfonyl esters at room temperature, it was deemed unnecessary to conduct VT NMR experiments for the other compounds. It was clear that the larger auxiliary (amino acid) slowed the rotation better than the smaller one (camphor) and therefore, dendrimers without any auxiliaries present would rotate even more rapidly.
3.7 Axial Chirality of Hexaaryl Dendrimers

As described previously in Chapter 2, hexaaryl dendrimers are categorised into two types based on the position of the substituents on rings G/G’, the parent-type dendrimers and the functionalised dendrimers. The presence of atropisomers in hexaaryl dendrimers is more evident in pyridyl-containing dendrimers as opposed to any of the parent-type dendrimers. In order to investigate further the effects of the ‘gearing’ aryl group, fluorine-containing functionalised dendrimers were designed with the position of the fluorines on these dendrimers proposed so that the resulting dendrimers represent both the parent-type dendrimer and the pyridyl-containing functionalised dendrimers.

In hexaaryl dendrimers, it was initially thought that since the presence of rings G/G’ would potentially hamper the free rotation, atropisomer resolution might be achieved. The evidence of this effect was obtained from the $^{19}$F NMR spectra of fluorine-containing symmetrical and unsymmetrical dendrimers (Section 2.7 in Chapter 2). These showed multiple $^{19}$F peaks, indicating that dendrimer arm rotations were slow enough to permit spectroscopic observation. Notwithstanding that, it was found that the separation of atropisomers was not achieved, and it was thought that the rotation must have still taken place despite the presence of rings G/G’. Therefore, attempts to study the axial chirality were performed on the mixture of atropisomers instead.

The interconversion between atropisomers in hexaaryl dendrimers was much slower than in pentaaryl dendrimers and therefore was not suitable for study using 1D VT NMR; instead, 2D $^{19}$F–$^{19}$F EXSY experiments were performed. These experiments were used for qualitative analysis by constructing an exchange map between the exchanging peaks and then deriving the rationale based on the resulting map. They were also used for quantitative analysis to obtain the kinetic and thermodynamic parameters. For the quantitative analysis of the main dendrimers, EXSY with varying mixing times at 298 K were used to obtain more accurate results. VT EXSY coupled with varying mixing times were performed to two of the main dendrimers (168 and 171) to study their properties at different temperatures. The quantitative analyses of the remaining dendrimers were performed to EXSY experiments with a single mixing time. All EXSY spectra and their analysis results are available in Appendix F.

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$^i$ 2D $^{19}$F–$^{19}$F EXSY experiments were performed either by the author or Dr Matthew Cliff, Senior Experimental Officer, The University of Manchester.

$^v$ VT $^{19}$F–$^{19}$F EXSY experiments were performed by Dr Ralph Adams, Research Fellow in NMR Spectroscopy, Morris Group, The University of Manchester.
In an attempt to assign the atropisomers to the $^{19}$F NMR and 2D $^{19}$F–$^{19}$F EXSY results, a flowchart (Figure 3-18) was developed. Several possible suggestions for peak assignments can be proposed by following this flowchart. Combined with the results obtained from other analyses, the peaks assignment could be performed. Although the
assignment of some dendrimers could not be achieved due to complications explained in the later part of this chapter, this method managed to explain the rationale for the $^{19}$F NMR results; which in turn gave valuable insight into the behaviour of the atropisomers.

The first stage of the atropisomer assignment as described in the flowchart was to draw the possible conformers and to rotate each of the structures $180^\circ$ about the middle axis (Scheme 3-1 (a)). This was performed to determine the pair of conformers that were meso compounds. After the meso compounds were identified, stereochemical configuration ($P$ or $M$) for each conformer was performed to determine pairs of enantiomers and diastereomers.

![Scheme 3-1 Two types of rotations performed to the dendrimers.](image)

The next stage was to determine the number of distinguishable species. One pair of meso compounds was considered to be one species. One pair of atropoenantiomers was also considered to be one species as they are indistinguishable by NMR. Determination of the total number of peaks each species gives rise to was then performed. A species with a plane of symmetry or an axis of symmetry gave one $^{19}$F peak, whilst species without any symmetry (dissymmetrical species) gave two $^{19}$F peaks. The result was then compared to the experimental $^{19}$F NMR result.

Aside from the determination of the total number of species and peaks, representational dendrimer arms movement simulation was also performed to establish the relationship amongst each atropisomer as a result of the actual dendrimer arm rotations (Scheme 3-1 (b)). It was found that when different arms in each atropisomer move twice, a group of atropisomers that interconvert amongst each other can be established. Following this, a theoretical correlation was established and compared to the experimental 2D $^{19}$F–$^{19}$F
EXSY result. Using this result as well as the consideration obtained previously from the 
$^{19}$F NMR, atropisomer assignment was proposed.

Following the assignment, experimental and computational calculations of the thermodynamic parameters of the processes were performed. The values obtained from the computational calculation were compared to those obtained from the experimental 2D $^{19}$F–$^{19}$F EXSY in an attempt to confirm the atropisomer assignment that had been established by following the flowchart. Other analyses, which are explored further in the following sections of this chapter, were also performed to aid assignment.

### 3.7.1 Atropisomers of Para-substituted Dendrimer System

There are two chiral axes in *para*-substituted dendrimers and therefore, they can exist as four atropisomers, regardless of whether they are symmetrical or unsymmetrical. These atropisomers, along with their respective stereochemical configuration, are summarised in Figure 3-19.

![Figure 3-19 Atropisomers and configurations in a general *para*-substituted dendrimer system.](image)

The same atropisomers were present in pentaaryl dendrimers as discussed in Section 3.5, but were not observable spectroscopically due to fast dendrimer arm rotations. In the *para*-substituted dendrimer, these atropisomers were observable due to slower rotation. Moreover, the presence of fluorine as a reporter has made it easier to observe the atropisomers of hexaaryl dendrimers.

Rotation of any dendrimer arm of any of these atropisomers results in interconversion with another atropisomer. Depending on which arm moves, one atropisomer can form two different atropisomers. If followed by the movement of the other arm, these two atropisomers would end up forming the same atropisomer. This is shown more clearly through the arm simulation summarised in Scheme 3-2.
Following the dendrimer arms simulation, a theoretical exchange map that connects all of these atropisomers to one another can be constructed. Since this network forms a square, it is referred to as ‘Para Exchange Square’ (Scheme 3-2).

For simplification, the top left atropisomers are assumed as the ‘starting point’ in each square; although in reality any atropisomer could be used as a starting point. The exchange squares are named based on the system they represent and on their respective starting point; thus the square shown in Scheme 3-2 for the para-system is referred to more specifically as Para Exchange Square-‘a’. This naming system is also used for more specific exchange squares derived from these squares.

Some of the interconversions between these atropisomers may be obscured depending on whether or not pairs of atropoenantiomers and meso compounds are present. Nevertheless, the simulation is useful to illustrate the para-substituted system in general and as a method to derive more specific exchange squares, especially when unsymmetrical systems are involved. This will be described in the latter part of this thesis.
3.7.2 Atropisomers of Ortho-substituted Dendrimer System

There are four chiral axes in ortho-substituted dendrimers and therefore, they can exist as 16 different atropisomers regardless of whether they are symmetrical or unsymmetrical. All of the possible atropisomers, along with their respective stereochemical configurations, are shown in Figure 3-20.

![Figure 3-20 Atropisomers and configurations in a general ortho-substituted dendrimer system.](image)

Similar to the para-substituted system, rotation of one dendrimer arm may result in the formation of two possible atropisomers and the second arm rotation would give the same atropisomers. The arm simulation of ortho-substituted dendrimer is shown in (Scheme 3-3) and four theoretical exchange squares were constructed based on the simulation result. The atropisomers in each of the squares exchange with one another but they do not form atropisomers that belong to other squares, because to do so requires rotation of fluorobenzene rings, which is a high energy process. This will be described in Section 3.7.3.
Similar to the para-substituted system, some of these exchanges may be obscured depending on whether or not atropoenantiomers or meso compounds are present. Nevertheless, these squares are useful to illustrate the ortho-substituted system in general and as a reference to derive more specific exchange squares, especially when unsymmetrical systems are involved.
3.7.3 Rotation of Fluorobenzene Rings in Para and Ortho Systems

The ortho system has four chiral axes, two of which are the dendrimer arms, whilst the other two are the axes of rings G/G’. Rotation of these axes in the ortho system gives another atropisomer. On the contrary, these axes in the para system are achiral and therefore their rotation does not result in a different atropisomer.

\[ \Delta G^\ddagger = 97.1 \text{ kJ mol}^{-1}, \]
\[ \Delta H^\ddagger = 85.4 \text{ kJ mol}^{-1}, \]
\[ k = 5.93 \times 10^6 \text{ s}^{-1}. \]

**Figure 3-21** Rotation of fluorobenzene ring in both systems and their respective energy barriers at 298 K revealed through DFT calculation.

DFT calculation was performed at M06-2X/6-31G** level of theory to atropisomer a for the para system and atropisomer b for the ortho system (Figure 3-21), revealing that the process for the ortho system was higher in energy than the para system. The rotation of the fluorobenzene ring is a high energy process since it requires the electronegative fluorine atom to rotate past the very proximate \( \pi \)-electron cloud of the neighbouring aromatic rings. Moreover, the difference in size between fluorine and hydrogen may also contribute to steric hindrance. This suggested that the fluorobenzene ring rotation in the ortho system was too slow to be observable in EXSY and thus was not taken into account during the arm movement simulation (Scheme 3-3).

3.7.4 Axial Chirality of Symmetrical Hexaaryl Dendrimers

Two dendrimers were used to represent the symmetrical para-substituted and ortho-substituted families: dendrimers 168 and 171 respectively (Figure 3-22). As explained previously, other analogues of these dendrimers have also been synthesised, such as those that contain peripheral fluorines (dendrimers 169 and 172) and a central hydroxy group (dendrimers 170 and 173). However, due to their structural similarity, only dendrimers 168 and 171 were chosen as the main compounds for this study.

Both of these dendrimers were subjected to 2D \( ^{19} \text{F} - ^{19} \text{F} \) EXSY experiments to map the
experimental exchange network between the $^{19}$F peaks. EXSY experiments with varying mixing times were performed to establish interconversion rate constants. Furthermore, VT EXSY with varying mixing times were performed to both dendrimers to obtain the kinetic and thermodynamic parameters at different temperatures.

![Hexa-H-(4-Fluorophenyl)-Br-Br 168](image1)

![Hexa-H-(2-Fluorophenyl)-Br-Br 171](image2)

**Figure 3-22** Symmetrical dendrimers that are used as models in this study.

### 3.7.4.1 Axial Chirality of Para-substituted Symmetrical Hexaaryl Dendrimers

Previously shown in Figure 2-32 in Chapter 2, the $^{19}$F NMR spectrum of dendrimer 168 revealed two peaks, indicating the presence of atropisomers. In order to study the exchange between the two peaks, 2D $^{19}$F-$^{19}$F EXSY was performed (Figure 3-23).

![2D $^{19}$F-$^{19}$F EXSY spectrum (470 MHz) of dendrimer 168. Bottom right inset shows the overall correlation between the two $^{19}$F peaks.](image3)

**Figure 3-23** 2D $^{19}$F-$^{19}$F EXSY spectrum (470 MHz) of dendrimer 168. Bottom right inset shows the overall correlation between the two $^{19}$F peaks. (F2 = F1 = $^{19}$F NMR)

The $^{19}$F-$^{19}$F EXSY result shows an exchange correlation between the two $^{19}$F peaks.
This indicates all species that give rise to peak 1 interconvert via dendrimer arm rotation, to form the other species that give rise to peak 2. To explain the rationale behind this observation, atropisomer assignment was performed using the method described previously in the flowchart. All of the possible atropisomers of dendrimer 168 have been shown in Figure 3-19. Their 180° rotation results and their relationship to other atropisomers are summarised in Table 3-3 below.

<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>180° Rotation Result</th>
<th>Atropisomer Relationship to other Atropisomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meso of b</td>
<td>Atropodiastereomer of c and d</td>
<td></td>
</tr>
<tr>
<td>Meso of a</td>
<td>Atropodiastereomer of c and d</td>
<td></td>
</tr>
<tr>
<td>Atropoenantiomer of d</td>
<td>Atropodiastereomer of a and b</td>
<td></td>
</tr>
<tr>
<td>Atropoenantiomer of c</td>
<td>Atropodiastereomer of a and b</td>
<td></td>
</tr>
</tbody>
</table>

Table 3-3 The relationships amongst atropisomers of dendrimer 168.

Determination of the total number of distinguishable species was performed by analysing the atropisomer relationships obtained from Table 3-3.

- Atropisomers a and b are meso and therefore indistinguishable in NMR: one species.
Axial Chirality and Conformational Studies

- Atropisomers c and d are a pair of atropoenantiomers and therefore indistinguishable in NMR: one species.
- As a whole, atropisomers a and b (although meso) are the atropodiastereomers of atropisomers c and d and therefore distinguishable in NMR: two species.
- Total number of distinguishable species in dendrimer 168: two species.

Determination of the total number of distinguishable peaks was performed by analysing the atropisomer structure in Table 3-3.
- Atropisomers a and b (one species) possess planes of symmetry and therefore each gives rise to one peak indistinguishable from each other.
- Atropisomers c and d (one species) possess axes of symmetry \(C_2\) and therefore each gives rise to one peak indistinguishable from each other.
- As a whole, atropisomers a and b are the atropodiastereomers of atropisomers c and d and therefore the peaks to which they give rise are distinguishable from each other in NMR.
- Total number of distinguishable peaks: two peaks.

As shown in Figure 3-23, the \(^{19}\text{F}\) NMR spectrum of dendrimer 168 showed that there are two peaks, which is in agreement with the proposed result above.

The simulation of dendrimer arm movement for the para-substituted system and the resulting Para Exchange Square (Scheme 3-2) have been previously discussed. It is now established from the results in Table 3-3, that atropisomers a and b are meso compounds, and atropisomers c and d are a pair of atropoenantiomers. Taking into account these observations, the Para Exchange Square-‘a’ can be derived to a final correlation between atropisomers shown in Scheme 3-4 (b).

\[
\begin{align*}
\text{Atropisomers a/b} &= \text{meso} : 1 \text{ peak} \\
\text{Atropisomers c/d} &= \text{enantiomers} : 1 \text{ peak}
\end{align*}
\]

\[\text{Scheme 3-4} \quad (a) \text{ Para Exchange Square-‘a’}; \quad (b) \text{ Final correlation after taking into account the presence of meso compounds and atropoenantiomers.}\]
This result is in agreement with the $^{19}\text{F}-^{19}\text{F}$ EXSY spectrum of dendrimer 168 (Figure 3-23). Peak assignment was difficult as both peaks could originate from either atropisomers a/b or c/d. Fortunately, DFT calculations revealed that the conformers with $C_2$ symmetry (c/d) had the lowest energy amongst the three isomers. This indicated that atropisomers c/d were the ones that gave rise to peak 2, as this peak has a slightly higher population than peak 1. To investigate this experimentally, the dendrimer was subjected to EXSY measurements at a range of temperatures and varying mixing times, and quantitative analysis was performed to obtain kinetic and thermodynamic parameters (Table 3-4).

![Diagram](image)

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>$k_{12}$ (s$^{-1}$)</th>
<th>$k_{21}$ (s$^{-1}$)</th>
<th>$\Delta G^\circ_{12}$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(12)}$ (s)</th>
<th>$\Delta G^\circ_{21}$ (kJ mol$^{-1}$)</th>
<th>$\Delta G^\circ_{21}$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(21)}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>273</td>
<td>0.025</td>
<td>0.020</td>
<td>75.05</td>
<td>27.92</td>
<td>489.16</td>
<td>75.54</td>
<td>34.64</td>
</tr>
<tr>
<td>283</td>
<td>0.049</td>
<td>0.040</td>
<td>76.28</td>
<td>14.14</td>
<td>470.63</td>
<td>76.76</td>
<td>17.27</td>
</tr>
<tr>
<td>293</td>
<td>0.220</td>
<td>0.172</td>
<td>75.41</td>
<td>3.15</td>
<td>594.08</td>
<td>76.00</td>
<td>4.02</td>
</tr>
<tr>
<td>298$^a$</td>
<td>0.365</td>
<td>0.294</td>
<td>75.48</td>
<td>1.90</td>
<td>540.09</td>
<td>76.02</td>
<td>2.36</td>
</tr>
<tr>
<td>303</td>
<td>0.668</td>
<td>0.564</td>
<td>75.27</td>
<td>1.04</td>
<td>425.03</td>
<td>75.69</td>
<td>1.23</td>
</tr>
<tr>
<td>313</td>
<td>1.892</td>
<td>1.568</td>
<td>75.13</td>
<td>0.37</td>
<td>488.63</td>
<td>75.61</td>
<td>0.44</td>
</tr>
<tr>
<td>323</td>
<td>4.676</td>
<td>3.875</td>
<td>75.18</td>
<td>0.15</td>
<td>504.53</td>
<td>75.69</td>
<td>0.18</td>
</tr>
</tbody>
</table>

$^a$ DFT calculation at M06-2X/6-31G** level of theory at 298 K estimated a value of $\Delta G^\circ = 82.6$ kJ mol$^{-1}$ ($\Delta H^\circ = 77.2$ kJ mol$^{-1}$) for the reverse process (2 $\rightarrow$ 1).

Table 3-4 General potential energy surface for the exchange in dendrimer 168 and results obtained from quantitative analysis of 2D $^{19}\text{F}-^{19}\text{F}$ EXSY at various temperatures. The forward process is assumed as peak 1 $\rightarrow$ 2, whilst the reverse process as 2 $\rightarrow$ 1.

![Figure 3-24](image)

**Figure 3-24** $^{19}\text{F}$ NMR spectrum (470 MHz) of 168 assigned to their respective atropisomers.
Experimental values confirmed that peak 2 had the lowest energy and it was therefore concluded that atropisomers c/d correspond to this peak. Consequently, the pair of meso compounds a/b correspond to peak 1 (Figure 3-24).

The rate constants obtained at each temperature from quantitative EXSY analysis were also used to construct Arrhenius and Eyring plots (Table 3-5).

<table>
<thead>
<tr>
<th>Process</th>
<th>( A ) (s(^{-1}))</th>
<th>( E_a ) (kJ mol(^{-1}))</th>
<th>( \Delta H^\circ ) (kJ mol(^{-1}))</th>
<th>( \Delta S^\circ ) (J mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forward</td>
<td>( 4.15 \times 10^{13} )</td>
<td>80.10</td>
<td>77.64</td>
<td>7.52</td>
</tr>
<tr>
<td>Reverse</td>
<td>( 4.17 \times 10^{13} )</td>
<td>80.62</td>
<td>78.15</td>
<td>7.56</td>
</tr>
</tbody>
</table>

Table 3-5 Results obtained from Arrhenius and Eyring plots for 168.

In summary, atropisomers of the para system have been successfully assigned using the method described by the flowchart, \(^{19}\)F–\(^{19}\)F EXSY and computational modelling.

3.7.4.2 Axial Chirality of Ortho-substituted Symmetrical Hexaaryl Dendrimers
As previously discussed the \(^{19}\)F NMR spectrum of dendrimer 171 showed eight peaks (Figure 2-36 in Chapter 2). This indicated that there were more atropisomers in the ortho system as opposed to the para system. To study the chemical exchange caused by the rotation of the dendrimer arms, 2D \(^{19}\)F–\(^{19}\)F EXSY was performed (Figure 3-25).

Figure 3-25 2D \(^{19}\)F–\(^{19}\)F EXSY spectrum (470 MHz) of dendrimer 171. (F2 = F1 = \(^{19}\)F NMR)
The $^{19}$F-$^{19}$F EXSY spectrum shows that the eight $^{19}$F peaks can be separated into two sets of four peaks (red and green). Each set of four peaks is referred to as an ‘exchange network’. The peaks within one exchange network show exchange correlation among each other, however, no correlation was observed between the two exchange networks, indicating that they belong to different systems.

Both exchange networks obtained from the EXSY can be mapped, revealing two squares labelled as EXSY Square ‘1’ and ‘2’, (Scheme 3-5). The naming system for the EXSY Square follows the same system for the Exchange Square.

![Scheme 3-5 Peaks exchange correlations of dendrimer 171 obtained from 2D $^{19}$F-$^{19}$F EXSY result showing two sets of four peaks labelled as EXSY Square ‘1’ and ‘2’.

Cross peaks between peaks 1 ⇋ 7, 3 ⇋ 5, 2 ⇋ 6 and 4 ⇋ 8 could be observed in the spectra recorded at longer mixing times. These cross peaks were not observed at shorter mixing times, indicating that they arose from sequential exchange (e.g. 1 ⇋ 3 ⇋ 7).vi They were not observed at shorter mixing times because the exchange was slow and only observable at longer mixing times.

In order to better explain the rationale behind this observation, atropisomer assignment of ortho-substituted dendrimer 171 was performed using the methodology described previously in the flowchart. All of the possible atropisomers of dendrimer 171 have been shown in Figure 3-20. Their 180° rotation results and their relationships to other atropisomers are summarised in Table 3-6.

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vi Personal communication with Prof Gareth A Morris, Professor of Physical Chemistry, The University of Manchester.
<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>180° Rotation Result</th>
<th>Atropisomer Relationship to other Atropisomers</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /> a (P, M, M, P)</td>
<td><img src="image2.png" alt="Image" /> e (M, P, P, M)</td>
<td><em>Meso</em> of each other Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image3.png" alt="Image" /> b (P, M, P, M)</td>
<td><img src="image4.png" alt="Image" /> f (M, P, M, P)</td>
<td><em>Meso</em> of each other Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image5.png" alt="Image" /> c (P, M, M, M)</td>
<td><img src="image6.png" alt="Image" /> g (M, P, M, M)</td>
<td><em>Meso</em> of each other Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image7.png" alt="Image" /> d (P, M, P, P)</td>
<td><img src="image8.png" alt="Image" /> h (M, P, P, P)</td>
<td><em>Meso</em> of each other Atropoenantiomer of d and h Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image9.png" alt="Image" /> i (P, P, M, M)</td>
<td><img src="image10.png" alt="Image" /> i (P, P, M, M)</td>
<td>Atropoenantiomer of m Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image11.png" alt="Image" /> j (P, P, P, P)</td>
<td><img src="image12.png" alt="Image" /> j (P, P, P, P)</td>
<td>Atropoenantiomer of n Atropodiastereomer of the rest</td>
</tr>
<tr>
<td><img src="image13.png" alt="Image" /> k (P, P, M, P)</td>
<td><img src="image14.png" alt="Image" /> l (P, P, P, M)</td>
<td><em>Meso</em> of each other Atropoenantiomer of o and p Atropodiastereomer of the rest</td>
</tr>
</tbody>
</table>
There are several atropisomeric pairs that are unique with this dendrimer. Atropisomers c and g are meso compounds, but they are also the atropoenantiomer of atropisomers d and h; whilst atropisomers d and h are themselves meso compounds. This also applies for atropisomers k and l (meso compounds) which are the atropoenantiomer of atropisomers o and p (meso compounds). Understanding this relationship between isomers was crucial in the determination of the total number of species and peaks.

Determination of the total number of distinguishable species was performed by analysing the atropisomer relationship obtained from Table 3-6.

- Atropisomers that are meso compounds and therefore indistinguishable in NMR:
  - Atropisomers a and e: one species.
  - Atropisomers b and f: one species.
- Atropisomers that are pairs of atropoenantiomers and therefore indistinguishable in NMR:
  - Atropisomers i and m: one species.
  - Atropisomers j and n: one species.
- Atropisomers that are meso compounds and are also the atropoenantiomers of other atropisomers and therefore indistinguishable in NMR:
  - Atropisomers c/g and d/h: one species.
  - Atropisomers k/l and o/p: one species.
As a whole, each pair of meso compounds and/or atropoenantiomers is the atropodiastereomer of the rest of the species and therefore each of them is distinguishable from each other in NMR.

- Total number of distinguishable species in dendrimer 171: six species.

Determination of the total number of distinguishable peaks was performed by analysing the atropisomer structure in Table 3-6.

- Atropisomers that are meso compounds with planes of symmetry:
  - Atropisomers a and e: one peak.
  - Atropisomers b and f: one peak.
  - Both pairs of atropisomers are the atropodiastereomers of each other; therefore, this group of two pairs of atropisomers gives rise to two distinguishable peaks in total.

- Atropisomers that are atropoenantiomers with axes of symmetry (C2):
  - Atropisomers i and m: one peak.
  - Atropisomers j and n: one peak.
  - Both pairs of atropisomers are the atropodiastereomers of each other; therefore, this group of two pairs of atropisomers gives rise to two distinguishable peaks in total.

- Atropisomers that are meso compounds and are also atropoenantiomers but possess neither plane nor axis of symmetry (dissymmetric):
  - Atropisomers c/g and d/h: two distinguishable peaks.
  - Atropisomers k/l and o/p: two distinguishable peaks.
  - Both of the two pairs of atropisomers are the atropodiastereomers of each other; therefore, this group of four pairs of atropisomers gives rise to four distinguishable peaks in total.

- As a whole, each pair of meso compounds and/or atropoenantiomers is the atropodiastereomer of the rest of the species and therefore the peaks they give rise to are distinguishable from each other in NMR.

- Total number of distinguishable peaks: eight peaks.

As also shown previously, 19F NMR spectrum of dendrimer 171 showed eight peaks in. This shows that the theoretical assignments are in agreement with what is observed experimentally.
The simulation of dendrimer arms movement for the ortho-substituted system and the resulting Ortho Exchange Squares have been established (Scheme 3-3). It has now been determined from the results in Table 3-6, that there are pairs of meso compounds, atropoenantiomers as well as combinations of both meso and atropoenantiomers. Taking into account these observations, the final atropisomer correlation of 171 shows two sets of four exchanging peaks (Scheme 3-6 (b)).

![Scheme 3-6](image)

This result is in agreement with the $^{19}$F–$^{19}$F EXSY result of dendrimer 171, previously (Figure 3-25), which also showed two exchange squares. These squares are labelled as Ortho Exchange Square-‘a/e’ and Ortho Exchange Square-‘i/m’, using the atropisomer starting point as the reference.

In order to perform atropisomer assignment in the ortho system, it was necessary to compare the $^{19}$F NMR spectrum of this dendrimer with its unsymmetrical analogue (189) (previously shown in Figure 2-42 in Chapter 2). The first set of two $^{19}$F peaks in dendrimer 189 exhibited through-space coupling. DFT calculation of the $^{19}$F–$^{19}$F nuclei distance in Table 2-15 and computational modelling of atropisomers revealed that the only conformers that may give rise to this behaviour were those that possess $C_2$ symmetry. These conformers, following atropisomer labelling in Figure 3-20, are atropisomers i and m.

Translating this observation to symmetrical system, dendrimer 171, peak 1 in the $^{19}$F NMR spectrum would belong to atropisomers i/m which are a pair of atropoenantiomers.
Since atropisomers i/m belongs to Ortho Exchange Square-‘i/m’, and because peak 1 belongs to EXSY Square ‘1’, peak assignment can be performed by matching the atropisomers to the peaks in both squares. It has also been established previously by atropisomer relationship analysis that atropisomers c/d/g/h are indistinguishable and are counted as one species, giving rise to two distinguishable peaks. Combining this information, results in assignments shown in Scheme 3-7 (c).

This assignment shows that there were three NMR-distinguishable species that gave rise to EXSY Square 1 and they formed a three-site exchange network instead of a four-site. This is supported by other analysis further explained later in this section.

Since EXSY Square ‘1’ has been assigned to Ortho Exchange Square-‘i/m’, EXSY Square ‘2’ can only belong to Ortho Exchange Square-‘a/e’. It was thought that the position of the fluorines in atropisomers a/e made these species high in energy, giving rise to $^{19}$F peak with low populations (peak 2 in the $^{19}$F NMR spectrum). DFT calculation performed at M06-2X/6-31G** level of theory confirmed that amongst the species in Ortho Exchange Square-‘a/e’, atropisomers a/e were the highest in energy. Therefore, peak assignment could be performed (Scheme 3-8).
Similar to the other exchange network, the assignment shows that there were also three NMR-distinguishable species belonging to EXSY Square ‘2’. These species also formed a three-site exchange network, similar to those in the previous exchange network.

DFT calculation at M06-2X/6-31G** level of theory of atropisomers a/e also revealed that the fluorobenzene rings in this pair of conformers underwent rapid interchange at 298 K (Figure 3-26). Substituting $\Delta G^\circ$ to the Eyring equation, gave the rate constant and half-life of interchange of $3.43 \times 10^6 \text{s}^{-1}$ and $2.02 \times 10^7 \text{s}$.

In both Scheme 3-7 and Scheme 3-8, the dissymmetric species (atropisomers c/d/g/h and k/l/o/p) have been assigned to peaks 3, 4, 5 and 8. This means the pair of peaks to which each set of species gives rise should possess equal populations (integrals) at all temperatures: peak 3 and 5 should possess equal population, and similarly, peak 4 and 8 should also possess equal population. Lineshape fitting was performed to the $^{19}\text{F}$ NMR spectra of dendrimer 171 (and also to one of its analogues, dendrimer 173) at each temperature in order to obtain accurate integrals (Table 3-7). It was performed using the dcon module in Bruker TopSpin 3.1 software. The complete fitting results and integrals for all peaks and both dendrimers 171 and 173 are available in Appendix D.

![Figure 3-26 Rapid interchange of fluorobenzene rings in conformer a/e.](image)

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>Peaks 3/5 Area and Ratio</th>
<th>Peaks 4/8 Area and Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak 3</td>
<td>Peak 5</td>
</tr>
<tr>
<td>263</td>
<td>159.845</td>
<td>153.600</td>
</tr>
<tr>
<td>273</td>
<td>80.074</td>
<td>77.523</td>
</tr>
<tr>
<td>283</td>
<td>107.952</td>
<td>107.108</td>
</tr>
<tr>
<td>293</td>
<td>128.972</td>
<td>128.925</td>
</tr>
<tr>
<td>298</td>
<td>669.339</td>
<td>665.136</td>
</tr>
<tr>
<td>303</td>
<td>94.033</td>
<td>92.983</td>
</tr>
<tr>
<td>313</td>
<td>146.884</td>
<td>146.893</td>
</tr>
<tr>
<td>323</td>
<td>199.835</td>
<td>198.263</td>
</tr>
</tbody>
</table>

Table 3-7 Integral values of peaks 3/5 and 4/8 and their ratios in $^{19}\text{F}$ NMR spectra (470 MHz) of dendrimer 171 at various temperatures obtained through lineshape fitting.

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vi Personal communication with Prof Gareth A Morris, Professor of Physical Chemistry, The University of Manchester.
The presence of low-intensity $^{13}$C-satellites has made it difficult to obtain accurate integrals. From the results obtained for dendrimer 171 and 173 at various temperatures however, it was clear that the ratio of peaks 3/5 and 4/8 were the ones that were consistently the closest to 1:1 at all temperatures. This confirmed that peaks 3/5 and 4/8 originated from the dissymmetric species in dendrimer 171 and therefore also confirmed the assignment previously proposed for both EXSY squares. The atropisomer assignment to the $^{19}$F NMR spectrum is shown in Figure 3-27.

![Figure 3-27 $^{19}$F NMR spectrum (470 MHz) of 171 assigned to their respective atropisomers.](image)

Dendrimer 171 was also subjected to EXSY measurement at a range of temperatures with varying mixing times and quantitative analysis was performed to the resulting spectra. Unfortunately, only those recorded at 298, 303 and 313 K gave spectra with good enough S/N-ratio to enable observation and quantitative analysis. The results are summarised in Table 3-8.

Each three-site exchange network was broken into two sets of two-site exchange and the rate constants and energy barriers were calculated. It has been established that peaks 3/5 and 4/8 belong to one species each, and therefore the rate constants and $\Delta G^\neq$ barriers that were determined were of the interconversion between two exchanging species, rather than exchanging peaks (e.g. $1 \rightleftharpoons 3$ and $1 \rightleftharpoons 5$).

Some of the processes were also modelled computationally. Although the values obtained computationally were different from those obtained experimentally, they showed similar trends. For example, the $1 \rightleftharpoons 3/5$ exchange system, the forward process has a lower energy barrier compared to the reverse process.
Table 3-8 General potential energy surface for the atropisomer exchange in dendrimer 171 and results obtained from quantitative analysis of 2D $^{19}$F-$^{19}$F EXSY at various temperatures. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

In summary, atropisomers of the ortho system has been successfully assigned using the method described by the flowchart, $^{19}$F-$^{19}$F EXSY and computational modelling. The dendrimers in the ortho system exist as six NMR-distinguishable species, giving rise to eight peaks in the $^{19}$F NMR spectrum. The results obtained for this dendrimer is also applicable to its analogues (172 and 173) due to structural similarity.

3.7.5 Axial Chirality of Unsymmetrical Hexaaryl Dendrimers

Investigation of the chirality and conformational behaviour of hexaaryl dendrimers was also extended to the unsymmetrical dendrimers. The main difference between these and symmetrical systems, aside from the obvious difference in peripheral groups, is that meso compounds are not formed in the unsymmetrical dendrimers due to the symmetry.
breaking. The formation of meso compounds in symmetrical dendrimers has obscured several isomers, therefore, it was expected that the unsymmetrical dendrimers should enable the observation of these isomers.

The two main dendrimers employed to represent the unsymmetrical para-substituted and ortho-substituted families were dendrimers 187 and 189 respectively (Figure 3-28). Two analogues of these dendrimers, 188 and 190, possessing a hydroxy group on their central ring (ring A), have also been synthesised but due to the structural similarity, only 187 and 189 were chosen as the main compounds for the conformational studies.

![Figure 3-28 Unsymmetrical dendrimers that are used as models in this study.](image)

Atropisomer assignment of the unsymmetrical hexaaryl dendrimers also follows the methodology previously described in the flowchart (Figure 3-18), but several steps was omitted for these dendrimers. Since meso compounds were not formed, there was no need for each atropisomer to be rotated 180°. Moreover, since these dendrimers possess no plane or axis of symmetry, the number of peaks they give rise to are double the number of peaks of their symmetrical analogues.

### 3.7.5.1 Axial Chirality of Para-substituted Unsymmetrical Hexaaryl Dendrimers

The 19F NMR spectrum of dendrimer 187 showed eight peaks, four of which belong to the peripheral fluorines. The remaining 19F peaks belong to the central fluorines. Comparing the 19F NMR spectrum of this dendrimer with the spectra of its precursors, it was concluded that two of these 19F peaks belonged to the bromine side, and that the other two to the fluorine side. (Figure 2-41 in Chapter 2) This result was supported by the 19F–19F EXSY spectrum (Figure 3-29).
The $^{19}$F-$^{19}$F EXSY spectrum showed that the $^{19}$F peaks that belonged to the bromine side were interconverting with each other, which is also true for those which belonged to the fluorine side. However, as would be expected, it was observed that both sets of peaks did not interconvert with each other.

In order to explain the rationale behind this observation, atropisomer assignment of para-substituted dendrimer 187 was performed. Since these were unsymmetrical dendrimers, there were only pairs of atropoenantiomers and each pair was the atropodiastereomer of the rest (Table 3-9).

Determination of the total number of distinguishable species was performed by analysing the atropisomer relationship obtained from Table 3-9.

- Atropisomers that are pairs of atropoenantiomers and therefore indistinguishable in NMR:
  - Atropisomers a and b: one species.
  - Atropisomers c and d: one species.
- As a whole, atropisomers a and b are atropodiastereomers of atropisomers c and d and therefore both species are distinguishable in NMR: two species.
- Total number of distinguishable species in dendrimer 187: two species.

Determination of the total number of distinguishable peaks was performed by analysing the atropisomer structure in Table 3-9.

- There is no plane or axis of symmetry in any of the atropisomers.
- Atropisomers a and b (one species) give rise to two distinguishable peaks, one peak each for central fluorine on the Br- and F-sides.
- Atropisomers c and d (one species) give rise to two distinguishable peaks, one peak each for central fluorine on the Br- and F-sides.
- As a whole, atropisomers a and b are atropodiastereomers of atropisomers c and d and therefore give rise to four distinguishable peaks.
- Total number of distinguishable peaks: four peaks.

<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>Atropoenantiomer Pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Structure" /></td>
<td>(P, M)</td>
</tr>
<tr>
<td><img src="image2.png" alt="Structure" /></td>
<td>(M, P)</td>
</tr>
<tr>
<td><img src="image3.png" alt="Structure" /></td>
<td>(M, P)</td>
</tr>
<tr>
<td><img src="image4.png" alt="Structure" /></td>
<td>(P, M)</td>
</tr>
<tr>
<td><img src="image5.png" alt="Structure" /></td>
<td>(P, P)</td>
</tr>
<tr>
<td><img src="image6.png" alt="Structure" /></td>
<td>(M, M)</td>
</tr>
<tr>
<td><img src="image7.png" alt="Structure" /></td>
<td>(M, M)</td>
</tr>
<tr>
<td><img src="image8.png" alt="Structure" /></td>
<td>(P, P)</td>
</tr>
</tbody>
</table>

Table 3-9 Atropisomers and their respective atropoenantiomer pairs in dendrimer 187. Each pair of atropoenantiomer is the atropodiastereomer of the rest.
Axial Chirality and Conformational Studies

The $^{19}$F NMR result of dendrimer 187 showed four peaks for the central fluorines, indicating that the theoretical assignment is in agreement with experimental.

The simulation of arms movement for the para system and the resulting Para Exchange Square have been shown in Scheme 3-2. It has now been established, from the results in Table 3-9, that although there were no meso compounds, both atropisomers a and b and atropisomers c and d were atropoenantiomers of themselves and atropodiastereomers of each other. Taking into account this relationship, a final atropisomer correlation is shown in Scheme 3-9 (b), which is similar to what was obtained for its symmetrical analogue 168.

![Scheme 3-9 Para Exchange Square in unsymmetrical dendrimer 187. (a) Colour-coded according to the sides to which the moving arms belong; (b) Correlation after taking into account the pairs of atropoenantiomers; (c) The same interconversion between atropisomers can take place regardless of the side to which the moving arms belong. L and R indicate the arms that move. Purple and orange indicate the arm movements from the Br- and F-sides respectively.](image)

The $^{19}$F–$^{19}$F EXSY result of dendrimer 187 (Figure 3-29), indicated that there were two interconversions that originated from both Br- and F-sides. This could be clarified by looking at Scheme 3-9 (c) above. Regardless of the side to which the moving arm belonged, both atropisomers a and b still formed atropisomers c and d and vice versa. However, since the Br-side and the F-side gave rise to different $^{19}$F peaks, the $^{19}$F–$^{19}$F EXSY showed the correlation for each peak on each side, even though they represent interconversion of the same species.

Based on the comparison of $^{19}$F NMR spectra of this dendrimer with its symmetrical analogues (Figure 2-41 in Chapter 2) both $^{19}$F peaks of one unsymmetrical species should appear next to one another. Furthermore, judging by the structures of each atropoenantiomer pair, both fluorines in each pair (a/b or c/d) should exist in similar chemical environments and therefore should appear very close to each other.
The $^{19}$F peaks of the symmetrical analogue, dendrimer 168, have been assigned with the aid of computational modelling. Translating the results obtained for the symmetrical dendrimer to the unsymmetrical dendrimer 187, atropisomer assignment could be performed. Combining this with the explanation in the previous paragraphs, the final correlation obtained from the $^{19}$F–$^{19}$F EXSY spectrum and the atropisomer assignment for this dendrimer is shown in Scheme 3-10.

Quantitative analysis of the EXSY of this dendrimer was performed for the experiment run at a single mixing time at 0.40 s and at room temperature (298 K) (Table 3-10). This mixing time was chosen because it was found that the resulting values for this mixing time were close to those obtained from varying mixing times for the other dendrimers.

Quantitative analysis results showed that this dendrimer was not very different to the symmetrical dendrimers. They also confirmed the assignment by showing that the species that gave rise to peaks 3/4 have lower energy compared to those that gave rise to peaks 1/2.

### 3.7.5.2 Axial Chirality of Ortho-substituted Unsymmetrical Hexaaryl Dendrimers

Previously shown in Figure 2-42 in Chapter 2, the $^{19}$F NMR spectrum of dendrimer 189 showed 15 peaks. The first set of two peaks appeared as an AB quartet, whilst the remaining appeared to be pairs of singlets except for the last set of two peaks that overlapped and appeared as a singlet. Similar to the para unsymmetrical dendrimer system 187, each pair of $^{19}$F peaks belonged to the Br- and F-side. Unfortunately, it was
difficult to correctly differentiate between these in the ortho system \textbf{189}, because the distance between the two pairing peaks was too close.

In order to study the chemical exchange caused by the rotation of the dendrimer arms in dendrimer \textbf{189}, $^{19}\text{F} - ^{19}\text{F}$ EXSY was performed (Figure 3-30). Since the peaks appear very close to one another, EXSY was performed with $^1\text{H}$-decoupling in both dimensions. Additionally, resolution in the F1 dimension was increased so that even the closest pair of peaks could be resolved and analysed separately. The peripheral fluorine peaks are not shown so that the cross peaks of the central fluorines can be observed better.

![Figure 3-30 2D $^1\text{H}$-decoupled $^{19}\text{F} - ^{19}\text{F}$ EXSY spectrum (470 MHz) of unsymmetrical dendrimer \textbf{189}. Peripheral $^{19}\text{F}$ peaks are not shown for clarity. (F2 = F1 = $^{19}\text{F}$ NMR)](image)

The $^{19}\text{F} - ^{19}\text{F}$ EXSY spectrum showed four sets of four exchanging peaks. The peaks in each set do not interconvert with the peaks in the other sets. These are labelled as EXSY Square ‘1’, ‘2’, ‘3’ and ‘4’ (Scheme 3-11).

![Scheme 3-11 From left to right: EXSY Square ‘1’, ‘2’, ‘3’ and ‘4’ of dendrimer \textbf{189}.](image)
As previously explained for dendrimer 187, \(^{19}\text{F}\) peaks that were next to each other in the unsymmetrical system usually originated from one species and were therefore paired together. This could be extended further: by knowing that a pair of peaks belonged to one species, one can make an assumption which peak belongs to which side in that pair, in that species. Any peak may be assumed to belong to the \(\text{Br}\)-side as long as its pair is assumed to belong to the \(\text{F}\)-side. This assumption was mainly performed to simplify identification, mapping of the total exchange network, atropisomer assignment and quantitative analysis. It would not interfere in any way with any of the analysis.

An exception had to be made for peaks 5, 6, 9 and 10 (in EXSY Square ‘1’ and ‘2’) and 7, 8 and 15 (in EXSY Square ‘3’ and ‘4’). In the symmetrical analogue, there were two groups of dissymmetrical species that gave rise to four peaks different peaks in total, which are the equivalent of the aforementioned peaks in unsymmetrical dendrimer 189. Translating this to dendrimer 189, peak 5 was paired with peak 10, peak 6 with 9, peak 7 with 15 and peak 8 with 15. Therefore peak 15 was assumed to consist of two peaks from \(\text{Br}\)- and \(\text{F}\)-sides with equal populations, which was also supported by population ratio of other peaks obtained from lineshape fitting.

In this thesis, the peaks in EXSY Squares ‘1’ and ‘3’ were assumed to belong to the \(\text{Br}\)-side whilst those in EXSY Squares ‘2’ and ‘4’ to the \(\text{F}\)-side. Combining this with the other explanations in the previous paragraph, new EXSY Squares were derived (Scheme 3-12).

![Scheme 3-12 Peaks interconversion of dendrimer 189. Colour coding was only used to assume the side of the dendrimer to which each peak belongs. These squares are labelled as EXSY Square ‘1/2’ and EXSY Square ‘3/4’.

Atropisomer assignment was then attempted for this dendrimer. All of the possible conformations of dendrimer 189 and their configuration have been shown in Figure 3-20. The relationship among atropisomers is summarised in Table 3-11.
<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>Atropoenantiomer Pair</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>(P, M, M, P)</td>
</tr>
<tr>
<td>b</td>
<td>(P, M, P, M)</td>
</tr>
<tr>
<td>c</td>
<td>(P, M, M, M)</td>
</tr>
<tr>
<td>d</td>
<td>(P, M, P, P)</td>
</tr>
<tr>
<td>e</td>
<td>(M, P, P, M)</td>
</tr>
<tr>
<td>f</td>
<td>(M, P, M, P)</td>
</tr>
<tr>
<td>g</td>
<td>(M, P, M, P)</td>
</tr>
<tr>
<td>h</td>
<td>(M, P, P, P)</td>
</tr>
<tr>
<td>i</td>
<td>(P, P, M, M)</td>
</tr>
<tr>
<td>j</td>
<td>(P, M, M, M)</td>
</tr>
<tr>
<td>k</td>
<td>(P, P, P, P)</td>
</tr>
<tr>
<td>l</td>
<td>(M, M, P, M)</td>
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<tr>
<td>m</td>
<td>(M, M, M, M)</td>
</tr>
<tr>
<td>n</td>
<td>(P, P, P, P)</td>
</tr>
<tr>
<td>o</td>
<td>(M, M, P, M)</td>
</tr>
<tr>
<td>p</td>
<td>(M, M, M, P)</td>
</tr>
</tbody>
</table>

**Table 3-11** Atropisomers and their respective atropoenantiomer pairs of dendrimer 189. Each atropisomer is the atropodiastereomer of the rest, aside from its atropoenantiomer pair.
Determination of the total number of distinguishable species was performed by analysing the atropisomer relationship obtained from Table 3-11.

- Atropisomers that are pairs of atropoenantiomers and therefore indistinguishable in NMR:
  - Atropisomers a and e: one species.
  - Atropisomers b and f: one species.
  - Atropisomers c and h: one species.
  - Atropisomers d and g: one species.
  - Atropisomers i and m: one species.
  - Atropisomers j and n: one species.
  - Atropisomers k and o: one species.
  - Atropisomers l and p: one species.

- Each pair of atropoenantiomers is the atropodiastereomer of the rest and therefore all of them are distinguishable in NMR: eight species.

- Total number of distinguishable species in dendrimer 189: eight species.

Determination of the total number of distinguishable peaks was performed by analysing the atropisomer structure in Table 3-11.

- There is no plane or axis of symmetry in any atropisomers.
- Therefore, each species (one pair of atropoenantiomers) is dissymmetric and gives rise to two distinguishable peaks, one peak each side.
- As explained before, there are eight species; since each species gives rise to two distinguishable peaks, the total number of peaks: 16 peaks.
- Each pair of atropoenantiomers is the atropodiastereomer of the rest and therefore all of the peaks are distinguishable in NMR.
- Total number of distinguishable peaks: 16 peaks.

The simulation of dendrimer arms movement for the ortho-substituted system and the resulting Ortho Exchange Squares have been shown in Scheme 3-3. Since meso compounds were not formed, a slight difference in the resulting squares (compared to its symmetrical analogue) was observed in the final correlation (Scheme 3-13).
Axial Chirality and Conformational Studies

Scheme 3-13 Atropisomers correlation as a result of dendrimer arm movements. (a) Overall; (b) Final correlation after taking into account the atropoenantiomer pairs. Purple and orange indicate the arm movements from the Br- and F-sides respectively.

Since the meso compounds were not formed, the eight dissymmetric species, which were present in the symmetrical analogue 171, have become four pairs of atropoenantiomer (atropisomers c/h, d/g, k/o and l/p) in dendrimer 189. Because of this, it was difficult to determine which peaks these pairs of atropoenantiomers give rise to. Assignment of the rest of atropisomers, however, remains the same in this dendrimer as it was in its symmetrical analogue, as shown in Figure 3-31.

Figure 3-31 $^{19}$F peak assignment to atropisomers for dendrimer 189. Unequivocal assignment of peaks 5/10, 9/6, 7/15 and 15/8 could not be achieved due to lack of supporting data.

Quantitative analysis of the EXSY of this dendrimer was performed for the experiment at a single mixing time at 0.40 s and at room temperature (298 K) (Table 3-12). Since both exchange networks were four-site exchanges, each of them was broken into four sets of two-site exchanges. Although atropisomer assignment could only be performed
partially, peaks were paired by translating the results previously obtained from symmetrical 171 to unsymmetrical 189.

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^\ddagger$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$\Delta G_r$ (J mol$^{-1}$)</th>
<th>$\Delta G_r^\ddagger$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 $\equiv$ 5/10</td>
<td>0.035</td>
<td>0.035</td>
<td>81.28</td>
<td>19.75</td>
<td>37.57</td>
<td>81.32</td>
<td>20.05</td>
</tr>
<tr>
<td>5/10 $\equiv$ 12/14</td>
<td>0.199</td>
<td>0.161</td>
<td>76.98</td>
<td>3.48</td>
<td>521.52</td>
<td>77.50</td>
<td>4.29</td>
</tr>
<tr>
<td>12/14 $\equiv$ 6/9</td>
<td>0.147</td>
<td>0.183</td>
<td>77.73</td>
<td>4.71</td>
<td>-541.89</td>
<td>77.19</td>
<td>3.78</td>
</tr>
<tr>
<td>6/9 $\equiv$ 1/2</td>
<td>0.041</td>
<td>0.041</td>
<td>80.90</td>
<td>16.91</td>
<td>-17.20</td>
<td>80.88</td>
<td>16.79</td>
</tr>
<tr>
<td>3/4 $\equiv$ 7/15</td>
<td>0.252</td>
<td>0.053</td>
<td>76.40</td>
<td>2.75</td>
<td>3864.36</td>
<td>80.26</td>
<td>13.07</td>
</tr>
<tr>
<td>7/15 $\equiv$ 11/13</td>
<td>0.225</td>
<td>0.180</td>
<td>76.68</td>
<td>3.08</td>
<td>552.67</td>
<td>77.24</td>
<td>3.86</td>
</tr>
<tr>
<td>11/13 $\equiv$ 15/8</td>
<td>0.165</td>
<td>0.206</td>
<td>77.46</td>
<td>4.21</td>
<td>-558.56</td>
<td>76.90</td>
<td>3.36</td>
</tr>
<tr>
<td>15/8 $\equiv$ 3/4</td>
<td>0.059</td>
<td>0.281</td>
<td>79.99</td>
<td>11.71</td>
<td>-3858.46</td>
<td>76.13</td>
<td>2.47</td>
</tr>
</tbody>
</table>

Table 3-12: Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for dendrimer 189. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

The results were similar to those obtained for the equivalent species and processes in the symmetrical analogue 171.

### 3.8 Chiral Resolution Attempts of Hexaaryl Dendrimers

In an endeavour to achieve atropisomer separation, chiral auxiliaries were introduced to the hexaaryl dendrimers. Both parent-type and fluorine-containing hexaaryl dendrimers that possessed hydroxy functionality on the central core were subjected to esterification with amino acid chiral auxiliary 219 (Table 3-13).

![Diagram of hexaaryl dendrimer with amino acid chiral auxiliary 219](image)

<table>
<thead>
<tr>
<th>No.</th>
<th>Rings G/G' (Ar)</th>
<th>Rings D/E (X)</th>
<th>Rings D/E' (Y)</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>226</td>
<td>Phenyl</td>
<td>Br</td>
<td>Br</td>
<td>Hexa-OAaux-Phenyl-Br-Br</td>
<td>50</td>
</tr>
<tr>
<td>227</td>
<td>Phenyl</td>
<td>F</td>
<td>F</td>
<td>Hexa-OAaux-Phenyl-F-F</td>
<td>50</td>
</tr>
<tr>
<td>228</td>
<td>Phenyl</td>
<td>Br</td>
<td>F</td>
<td>Hexa-OAaux-Phenyl-Br-F</td>
<td>65</td>
</tr>
<tr>
<td>229</td>
<td>4-Fluorophenyl</td>
<td>Br</td>
<td>Br</td>
<td>Hexa-OAaux-(4-Fluorophenyl)-Br-Br</td>
<td>53</td>
</tr>
<tr>
<td>230</td>
<td>4-Fluorophenyl</td>
<td>Br</td>
<td>F</td>
<td>Hexa-OAaux-(4-Fluorophenyl)-Br-F</td>
<td>54</td>
</tr>
<tr>
<td>231</td>
<td>2-Fluorophenyl</td>
<td>Br</td>
<td>Br</td>
<td>Hexa-OAaux-(2-Fluorophenyl)-Br-Br</td>
<td>48</td>
</tr>
<tr>
<td>232</td>
<td>2-Fluorophenyl</td>
<td>Br</td>
<td>F</td>
<td>Hexa-OAaux-(2-Fluorophenyl)-Br-F</td>
<td>47</td>
</tr>
</tbody>
</table>

Table 3-13: Hexaaryl dendrimers with amino acid chiral auxiliaries attached 226-232.
Unlike pentaaryl dendrimers, esterification of hexaaryl dendrimers only gave moderate yields, possibly due to greater steric hindrance. Atropisomer resolution was not achieved even after the attachment of chiral auxiliaries, but spectroscopic observation of atropisomers was enabled, particularly those containing central fluorines. Qualitative and quantitative EXSY at room temperature was performed to these dendrimers to study their behaviour and derive both kinetic and thermodynamic parameters.

3.8.1 Esterification of Chiral Auxiliary to the Symmetrical and Unsymmetrical Parent-type Hexaaryl Dendrimers

Esterification of symmetrical and unsymmetrical parent-type hexaaryl dendrimers did not result in atropisomer resolution. Similar to the pentaaryl dendrimers, peak splittings were observed in the $^{13}$C NMR spectra of these esters. VT $^{13}$C NMR was not performed because the kinetic and thermodynamic parameters obtained from the fluorine-containing analogues would be similar to these dendrimers. Comparison of $^{13}$C NMR spectra between the esters and their respective precursors is shown in Figure 3-32.

![Figure 3-32](image-url) From top to bottom: a portion of of $^{13}$C NMR spectra (100 MHz) of 161, 226, 164, 227, 186 and 228. Similar to the pentaaryl dendrimers, splitting caused by the attachment of chiral auxiliary is evident.  = individual peaks or groups of peaks that were observed to have split upon chiral auxiliary attachment;  = chiral auxiliary aromatic peaks;  and  = peaks on rings D/D’/E/E’;  and  = peaks of the carbon on the para position relative to C–O in ring A. Purple and orange represent Br- and F-sides respectively.
3.8.2 Esterification of Chiral Auxiliary to the Symmetrical and Unsymmetrical Fluorine-containing Hexaaryl Dendrimers

Esterification was performed on the fluorine-containing dendrimers, both symmetrical and unsymmetrical, to spectroscopically study the resulting esters through $^{19}$F NMR and 2D $^{19}$F–$^{19}$F EXSY. The dendrimer arms rotation was too rapid to allow for resolution despite the addition of the chiral auxiliary.

Fluorine-containing hexaaryl dendrimers that possess a hydroxy functionality on the central ring were used: 170 and 173 for symmetrical para- and ortho-substituted hexaaryl dendrimers respectively, and 188 and 190 for the unsymmetrical analogues respectively (Figure 3-33).

![Figure 3-33](image)

Having a C–O group on the central ring (ring A) changes the stereochemical configuration assignment priority (Figure 3-34), but it does not change the species to which each atropisomer interconverts as a result of dendrimer arm rotations. The exchange network obtained from dendrimer arm movement simulation resulted in the same network of exchanging species and the same Para Exchange Square, as previously
shown in Scheme 3-2. Therefore, the Para Exchange Square–‘a’ still represents the overall network of exchanging species for the symmetrical and unsymmetrical esters.

![Figure 3-34](image)

**Figure 3-34** Atropisomers and configurations in para-substituted dendrimer system with chiral auxiliary attached on ring A. Blue A indicates amino acid auxiliary.

As with the para derivatives, the ortho-substituted ester system required a change to the stereochemical configuration assignment priority (Figure 3-35). This does not change the previously established exchange network obtained from arm movement simulation.

![Figure 3-35](image)

**Figure 3-35** Atropisomers and configurations in ortho-substituted dendrimer system with chiral auxiliary attached on ring A. Blue A indicates amino acid auxiliary.
Therefore, similar to the para ester system, Ortho Exchange Square-‘a’, ‘b’, ‘c’ and ‘d’ previously shown in Scheme 3-3 for ortho-substituted dendrimers are also applicable to the ortho-substituted ester system.

As opposed to the fluorine-containing dendrimers analysed thus far, full atropisomer assignment of fluorine-containing esters was difficult due to lack of supporting data. The attachment of chiral auxiliary converted enantiomers into diastereomers, and therefore each species was observable in NMR spectroscopy. This made atropisomer assignment more difficult. Computational modelling of this system should be performed in the future to aid the assignment.

3.8.2.1 Axial Chirality of Para-substituted Symmetrical and Unsymmetrical Hexaaryl Dendrimer Esters

The attachment of a chiral auxiliary gave rise to new peaks in the $^{19}\text{F}$ NMR spectrum. Comparison between the symmetrical and unsymmetrical esters with their respective precursors (Figure 3-36) eased the identification of peak origin.

![Figure 3-36](image-url)  
$^{19}\text{F}$ NMR spectra (470 MHz) comparison of esters 229 and 230 with their respective precursors. (▲ = peaks from Br-side; ▲ = peaks from F-side; ● = peripheral peaks)
From the $^{19}$F NMR result of symmetrical ester 229, it was theorised that the pair of meso compounds (a and b) may not have converted to diastereomers, but remained as meso. However, since one of the fluorines was closer to the aromatic ring of the chiral auxiliary moiety than the other, both fluorines would experience different chemical environments. The symmetry of the meso compounds could be broken in this manner, giving rise to two peaks. In this hypothesis, two peaks originated from the meso compound (a/b), whilst each of the two remaining peaks originated from the diastereomers with $C_2$ symmetry (c and d). Unfortunately, there is currently no method to prove this hypothesis. The total number of species in symmetrical ester 229 could not be determined. Computational studies of this ester and its ortho analogue (ester 231) should be performed in the future to aid with the interpretation of both $^{19}$F NMR and $^{19}$F–$^{19}$F EXSY results.

In the unsymmetrical ester 230, four species could be unambiguously determined since no meso compounds were formed. Moreover, because each species gives rise to two peaks (each originating from Br- and F-side), a total of eight peaks for the central fluorines was expected. This is in agreement with the observed $^{19}$F NMR spectrum.

![Diagram](image)

**Figure 3-37** $^1$H-decoupled $^{19}$F–$^{19}$F EXSY (470 MHz) of ester 229. ($F_2 = F_1 = ^{19}$F NMR)
To gain a picture of the interconversion among peaks, $^1\text{H}$-decoupled $^{19}\text{F}$–$^{19}\text{F}$ EXSY was performed to both the symmetrical (Figure 3-37) and unsymmetrical (Figure 3-38) esters. $^1\text{H}$-decoupling was performed in both dimensions to resolve peaks that were very close to each other. Unfortunately, peaks 2 and 3 in ester 229 and peaks 3 and 4 in ester 230 were only slightly resolved in the EXSY, even after decoupling. The resolution was enough for qualitative analysis but not for quantitative analysis.

The exchange network obtained from the $^{19}\text{F}$–$^{19}\text{F}$ EXSY spectrum of symmetrical ester 229 showed a four-site exchange (Scheme 3-14 (b)), which was the same as Para Exchange Square-‘a’ obtained from dendrimer arms simulation. The spectrum of the unsymmetrical ester 230 however, showed two sets of four-site exchange (Scheme 3-14 (c)). It has been established previously, from various examples and from the $^{19}\text{F}$ NMR spectra comparison of dendrimers 229, 230 and their precursors (Figure 3-36), that one species gives rise to two peaks, one belongs to the Br-side and the other one to the F-side. Therefore, both EXSY Squares can be combined to form either of the EXSY Squares shown in Scheme 3-14 (d).
Since the cross peaks between peaks 2 and 3 were obscured by the diagonal peaks, the intensities of the cross peaks could not be obtained. For the same reason, the actual intensities of the diagonal peaks 2 and 3 could not be obtained. Due to these difficulties, only the exchange between peaks 1 and 4 could be calculated. The quantitative analysis was performed using EXSY spectra recorded at 298 K with varying mixing time to obtain kinetic and thermodynamic parameters (Table 3-14).

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^2$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2}$ (s)</th>
<th>$\Delta G_r$ (J mol$^{-1}$)</th>
<th>$\Delta G_r^2$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2,r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ≠ 4</td>
<td>0.092</td>
<td>0.058</td>
<td>78.89</td>
<td>7.51</td>
<td>1138.36</td>
<td>80.03</td>
<td>11.88</td>
</tr>
</tbody>
</table>

Table 3-14 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and varying mixing time for dendrimer 229.

Based on the comparison between unsymmetrical ester 230 with symmetrical ester 229 and their respective precursors (Figure 3-36), only peaks 1/2 and 7/8 of 230 could be paired. Peaks 3/4/5/6 could not be paired due to lack of supporting data and therefore the two possible EXSY Squares were proposed (Scheme 3-14 (d)). Because of this and due to cross peaks 3 and 4 being obscured by the diagonal peaks in the EXSY spectrum, quantitative analysis was performed on the exchanging peaks rather than on the species, except for $1/2 \not= 7/8$. This exchange is the equivalent of $1 \not= 4$ in symmetrical ester 229. The kinetic and thermodynamic parameters were obtained from the EXSY spectrum.
recorded at 298 K and mixing time of 0.40 s (Table 3-15).

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 $\rceil$ 7/8</td>
<td>0.085</td>
<td>0.061</td>
<td>79.09</td>
<td>8.15</td>
<td>839.28</td>
<td>79.93</td>
</tr>
<tr>
<td>2 $\rceil$ 5</td>
<td>0.082</td>
<td>0.080</td>
<td>79.17</td>
<td>8.42</td>
<td>70.05</td>
<td>79.24</td>
</tr>
<tr>
<td>5 $\rceil$ 6</td>
<td>0.058</td>
<td>0.057</td>
<td>80.05</td>
<td>11.98</td>
<td>25.55</td>
<td>80.07</td>
</tr>
<tr>
<td>6 $\rceil$ 8</td>
<td>0.075</td>
<td>0.054</td>
<td>79.41</td>
<td>9.28</td>
<td>790.92</td>
<td>80.20</td>
</tr>
</tbody>
</table>

Table 3-15 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time of 0.40 s for dendrimer 230. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

In summary, the attachment of a chiral auxiliary to the para system revealed more peaks in the $^{19}$F NMR spectrum. When subjected to unsymmetrical dendrimer, eight $^{19}$F peaks that belong to the central fluorine were observed, indicating that each of the fluorines in each atropisomers had become NMR-distinguishable. Unfortunately, atropisomer assignment was not achieved and peak pairing in the unsymmetrical ester was only partially achieved due to lack of supporting data.

3.8.2.2 Axial Chirality of Ortho-substituted Symmetrical and Unsymmetrical Hexaaryl Dendrimers Esters

The attachment of a chiral auxiliary gave rise to new peaks in the $^{19}$F NMR spectrum. Comparison between the symmetrical and unsymmetrical esters (Figure 3-39) was performed to aid the identification of peak origin.

![Figure 3-39](image-url) $^{19}$F NMR spectra (470 MHz) comparison of symmetrical ester 231 (top) and unsymmetrical ester 232 (bottom). Peripheral $^{19}$F peaks of ester 232 are omitted for clarity.
There were 16 peaks observed in the $^{19}$F NMR spectrum of 231, two of which had low intensities. In the $^{19}$F NMR spectrum of unsymmetrical ester 232, two sets of two peaks exhibiting through-space coupling and two sets of two peaks with low intensities were observed out of a total of 32 peaks. These peaks suggest that there were two species with $C_2$ symmetry (giving rise to the peaks with through-space coupling) and two species with a plane of symmetry (giving rise to the low-intensity peaks) for each ester. This enabled partial peak assignment but the remaining peaks were problematic, particularly noticeable with symmetrical ester 231.

The species with planes of symmetry (atropisomers a, b, e and f) and $C_2$ symmetry (atropisomer i, j, m and n) account for eight peaks in ester 231. Using the information previously obtained from ortho-substituted dendrimers 171 and 189, atropisomers a and e were assigned to the peaks with low intensities. Atropisomers i and m were assigned to the peaks equivalent to those that exhibited through-space coupling in ester 232. This assignment also applies to the unsymmetrical ester 232. Unfortunately, the exact assignment could not be achieved due to lack of supporting data.

![Diagram](image)

**Figure 3-40** $^1$H-decoupled $^{19}$F–$^{19}$F EXSY (470 MHz) of ester 231. (F2 = F1 = $^{19}$F NMR)
In an attempt to assign the rest of the atropisomers that possess symmetry (b, f, j and n), it was necessary to know the exchange correlations among the $^{19}$F peaks, therefore $^{19}$F–$^{19}$F EXSY was performed to both esters. Similar to its para-substituted analogue, $^{19}$F–$^{19}$F EXSY with $^1$H-decoupling in both dimensions was performed to fully reveal the correlation between the peaks (Figure 3-40).

The result for symmetrical ester 231 showed four sets of four-site exchange network (Scheme 3-15).

![Scheme 3-15 Peaks exchange correlations of dendrimer 231 obtained from 2D $^{19}$F–$^{19}$F EXSY result showing four sets of four peaks.](image)

Each of the EXSY Squares started with either the low-intensity peaks (1 and 7) or peaks which exhibit through-space coupling in unsymmetrical analogues (2 and 3). The atropisomers that correspond to these peaks have been previously discussed, although the exact assignment could not be made. Following the exchange path in each EXSY Square, the remaining species that possessed symmetry could be assigned (peaks 9, 10, 11 and 14); meaning that the rest of the unassigned peaks belonged to the dissymmetrical species (Table 3-16).

<table>
<thead>
<tr>
<th>EXSY Squares</th>
<th>Symmetrical Peaks</th>
<th>Species</th>
<th>Dissymmetrical Peaks</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘1’</td>
<td>1</td>
<td>a or e</td>
<td>6</td>
<td>k or l or o or p</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>b or f</td>
<td>15</td>
<td>k or l or o or p</td>
</tr>
<tr>
<td>‘2’</td>
<td>2</td>
<td>i or m</td>
<td>4</td>
<td>c or d or g or h</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>j or n</td>
<td>13</td>
<td>c or d or g or h</td>
</tr>
<tr>
<td>‘3’</td>
<td>3</td>
<td>i or m</td>
<td>5</td>
<td>c or d or g or h</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>j or n</td>
<td>12</td>
<td>c or d or g or h</td>
</tr>
<tr>
<td>‘7’</td>
<td>7</td>
<td>a or e</td>
<td>8</td>
<td>k or l or o or p</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>b or f</td>
<td>16</td>
<td>k or l or o or p</td>
</tr>
</tbody>
</table>

Table 3-16 Partial assignment of ester 231.

For ester 231, quantitative analysis to extract the kinetic and thermodynamic parameters was performed to EXSY spectra recorded at 298 K with varying mixing times (Table 3-17). Since exact assignments could not be made, analysis was performed to the
exchanging peaks rather than exchanging species.

### Table 3-17

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G^o_f$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-(f)}$ (s)</th>
<th>$\Delta G_r$ (J mol$^{-1}$)</th>
<th>$\Delta G^o_r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-(r)}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (\rightarrow) 6</td>
<td>0.110</td>
<td>0.047</td>
<td>78.46</td>
<td>6.32</td>
<td>2103.80</td>
<td>80.56</td>
<td>14.77</td>
</tr>
<tr>
<td>6 (\rightarrow) 9</td>
<td>0.161</td>
<td>0.092</td>
<td>77.51</td>
<td>4.30</td>
<td>1390.55</td>
<td>78.90</td>
<td>7.54</td>
</tr>
<tr>
<td>9 (\rightarrow) 15</td>
<td>0.091</td>
<td>0.082</td>
<td>78.91</td>
<td>7.59</td>
<td>258.42</td>
<td>79.17</td>
<td>8.42</td>
</tr>
<tr>
<td>15 (\rightarrow) 1</td>
<td>0.040</td>
<td>0.180</td>
<td>80.99</td>
<td>17.53</td>
<td>-3751.04</td>
<td>77.24</td>
<td>3.86</td>
</tr>
<tr>
<td>2 (\rightarrow) 4</td>
<td>0.040</td>
<td>0.036</td>
<td>80.94</td>
<td>17.17</td>
<td>283.18</td>
<td>81.22</td>
<td>19.25</td>
</tr>
<tr>
<td>4 (\rightarrow) 10</td>
<td>0.119</td>
<td>0.080</td>
<td>78.26</td>
<td>5.83</td>
<td>992.60</td>
<td>79.25</td>
<td>8.70</td>
</tr>
<tr>
<td>10 (\rightarrow) 13</td>
<td>0.086</td>
<td>0.099</td>
<td>79.07</td>
<td>8.07</td>
<td>-348.84</td>
<td>78.72</td>
<td>7.01</td>
</tr>
<tr>
<td>13 (\rightarrow) 2</td>
<td>0.040</td>
<td>0.059</td>
<td>80.94</td>
<td>17.16</td>
<td>-930.09</td>
<td>80.01</td>
<td>11.79</td>
</tr>
<tr>
<td>3 (\rightarrow) 5</td>
<td>0.024</td>
<td>0.021</td>
<td>82.26</td>
<td>29.29</td>
<td>315.21</td>
<td>82.58</td>
<td>33.26</td>
</tr>
<tr>
<td>5 (\rightarrow) 14</td>
<td>0.064</td>
<td>0.063</td>
<td>79.79</td>
<td>10.79</td>
<td>53.00</td>
<td>79.84</td>
<td>11.03</td>
</tr>
<tr>
<td>14 (\rightarrow) 12</td>
<td>0.068</td>
<td>0.060</td>
<td>79.63</td>
<td>10.14</td>
<td>334.22</td>
<td>79.97</td>
<td>11.60</td>
</tr>
<tr>
<td>12 (\rightarrow) 3</td>
<td>0.027</td>
<td>0.036</td>
<td>81.90</td>
<td>25.32</td>
<td>-703.49</td>
<td>81.20</td>
<td>19.06</td>
</tr>
<tr>
<td>7 (\rightarrow) 8</td>
<td>0.115</td>
<td>0.032</td>
<td>78.33</td>
<td>6.00</td>
<td>3161.82</td>
<td>81.50</td>
<td>21.51</td>
</tr>
<tr>
<td>8 (\rightarrow) 11</td>
<td>0.092</td>
<td>0.085</td>
<td>78.90</td>
<td>7.54</td>
<td>186.98</td>
<td>79.08</td>
<td>8.13</td>
</tr>
<tr>
<td>11 (\rightarrow) 16</td>
<td>0.094</td>
<td>0.125</td>
<td>78.86</td>
<td>7.41</td>
<td>-724.38</td>
<td>78.13</td>
<td>5.53</td>
</tr>
<tr>
<td>16 (\rightarrow) 7</td>
<td>0.054</td>
<td>0.155</td>
<td>80.21</td>
<td>12.81</td>
<td>-2609.23</td>
<td>77.60</td>
<td>4.47</td>
</tr>
</tbody>
</table>

Table 3-17 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for dendrimer 231. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

**Figure 3-41** 2D $^1$H-decoupled $^{19}$F–$^{19}$F EXSY (470 MHz) of ester 232. (F2 = F1 = $^{19}$F NMR)
The EXSY result for unsymmetrical ester 232 is shown in Figure 3-41. The spectrum showed eight sets of four-site exchange networks, summarised Scheme 3-16.

![Scheme 3-16](image)

Scheme 3-16 Exchange correlation obtained from $^{19}$F--$^{19}$F EXSY. Difference in colour indicates different side to which each peak belongs.

Similar to the other unsymmetrical dendrimers and esters, one pair of two peaks must have arisen from one species. There were only certain peaks that could be unambiguously paired, which were those that possessed either a plane of symmetry or $C_2$ symmetry in symmetrical analogue 231 (Table 3-18). The rest of the peaks could not be paired due to ambiguity with dissymmetrical species as previously explained for symmetrical ester 231.

<table>
<thead>
<tr>
<th>Peaks</th>
<th>Species</th>
<th></th>
<th>Peaks</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2</td>
<td>a or e</td>
<td></td>
<td>5/6</td>
<td>i or m</td>
</tr>
<tr>
<td>17/18</td>
<td>b or f</td>
<td></td>
<td>27/28</td>
<td>j or n</td>
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<td>3/4</td>
<td>i or m</td>
<td></td>
<td>13/14</td>
<td>a or e</td>
</tr>
<tr>
<td>19/22</td>
<td>j or n</td>
<td></td>
<td>20/21</td>
<td>b or f</td>
</tr>
</tbody>
</table>

Table 3-18 Partial peak pairing and assignment for ester 232.

Unambiguous atropisomer assignment could not be achieved, even to peaks that could be paired due to the lack of supporting data. Future work should be attempted through computational calculation to aid atropisomer assignment. Peaks 3/4 and 5/6 in this ester (peaks 2 and 3 in symmetrical ester 231) arose from two species that possessed $C_2$ symmetry. Both pairs of peaks clearly have different intensities which means they have different populations and therefore different energy levels. Computational calculations should be able to aid with this assignment by determining the species that has a lower energy level.
Quantitative analysis of unsymmetrical ester 232 was performed using the EXSY that was recorded at 298 K and a mixing time of 0.40 s (Table 3-19). Since only partial peak pairing could be achieved, quantitative analysis was performed to the exchanging peaks instead of the exchanging species. Nevertheless, the trend for each pair of EXSY Squares (i.e. 1 and 2, 3 and 4, 5 and 6, 13 and 14) was similar.

<table>
<thead>
<tr>
<th>EXSY Squares</th>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^\circ$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_r^\circ$ (J mol$^{-1}$)</th>
<th>$\Delta G_r^\circ$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$t_{1/2-r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>'1'</td>
<td>1 $\Rightarrow$ 11</td>
<td>0.133</td>
<td>0.057</td>
<td>77.99</td>
<td>5.22</td>
<td>2082.08</td>
<td>80.07</td>
<td>12.10</td>
</tr>
<tr>
<td></td>
<td>11 $\Rightarrow$ 17</td>
<td>0.154</td>
<td>0.120</td>
<td>77.63</td>
<td>4.51</td>
<td>606.45</td>
<td>78.23</td>
<td>5.76</td>
</tr>
<tr>
<td></td>
<td>17 $\Rightarrow$ 30</td>
<td>0.097</td>
<td>0.082</td>
<td>78.76</td>
<td>7.12</td>
<td>419.86</td>
<td>79.18</td>
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</tr>
<tr>
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<td>30 $\Rightarrow$ 1</td>
<td>0.032</td>
<td>0.112</td>
<td>81.52</td>
<td>21.71</td>
<td>-3108.39</td>
<td>78.41</td>
<td>6.19</td>
</tr>
<tr>
<td>'2'</td>
<td>2 $\Rightarrow$ 12</td>
<td>0.153</td>
<td>0.061</td>
<td>77.63</td>
<td>4.52</td>
<td>2267.85</td>
<td>79.90</td>
<td>11.30</td>
</tr>
<tr>
<td></td>
<td>12 $\Rightarrow$ 18</td>
<td>0.121</td>
<td>0.096</td>
<td>78.22</td>
<td>5.72</td>
<td>567.06</td>
<td>78.78</td>
<td>7.20</td>
</tr>
<tr>
<td></td>
<td>18 $\Rightarrow$ 29</td>
<td>0.108</td>
<td>0.093</td>
<td>78.51</td>
<td>6.45</td>
<td>348.17</td>
<td>78.86</td>
<td>7.42</td>
</tr>
<tr>
<td></td>
<td>29 $\Rightarrow$ 2</td>
<td>0.029</td>
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<td>23.85</td>
<td>-3183.08</td>
<td>78.57</td>
<td>6.60</td>
</tr>
<tr>
<td>'3'</td>
<td>3 $\Rightarrow$ 7</td>
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<td>0.041</td>
<td>80.90</td>
<td>16.92</td>
<td>-6.10</td>
<td>80.89</td>
<td>16.88</td>
</tr>
<tr>
<td></td>
<td>7 $\Rightarrow$ 19</td>
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<td>0.110</td>
<td>78.18</td>
<td>5.65</td>
<td>264.32</td>
<td>78.45</td>
<td>6.28</td>
</tr>
<tr>
<td></td>
<td>19 $\Rightarrow$ 24</td>
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<td>0.103</td>
<td>78.91</td>
<td>7.58</td>
<td>-295.21</td>
<td>78.62</td>
<td>6.73</td>
</tr>
<tr>
<td></td>
<td>24 $\Rightarrow$ 3</td>
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<td>0.040</td>
<td>80.92</td>
<td>17.05</td>
<td>36.98</td>
<td>80.96</td>
<td>17.31</td>
</tr>
<tr>
<td>'4'</td>
<td>4 $\Rightarrow$ 8</td>
<td>0.045</td>
<td>0.046</td>
<td>80.67</td>
<td>15.45</td>
<td>-53.07</td>
<td>80.62</td>
<td>15.12</td>
</tr>
<tr>
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<td>8 $\Rightarrow$ 22</td>
<td>0.093</td>
<td>0.084</td>
<td>78.87</td>
<td>7.46</td>
<td>258.67</td>
<td>79.13</td>
<td>8.28</td>
</tr>
<tr>
<td></td>
<td>22 $\Rightarrow$ 26</td>
<td>0.102</td>
<td>0.114</td>
<td>78.65</td>
<td>6.83</td>
<td>-277.48</td>
<td>78.37</td>
<td>6.10</td>
</tr>
<tr>
<td></td>
<td>26 $\Rightarrow$ 4</td>
<td>0.032</td>
<td>0.031</td>
<td>81.51</td>
<td>21.61</td>
<td>71.87</td>
<td>81.58</td>
<td>22.24</td>
</tr>
<tr>
<td>'5'</td>
<td>5 $\Rightarrow$ 9</td>
<td>0.017</td>
<td>0.019</td>
<td>83.12</td>
<td>41.41</td>
<td>-284.98</td>
<td>82.83</td>
<td>36.91</td>
</tr>
<tr>
<td></td>
<td>9 $\Rightarrow$ 27</td>
<td>0.068</td>
<td>0.079</td>
<td>79.66</td>
<td>10.24</td>
<td>-390.65</td>
<td>79.26</td>
<td>8.74</td>
</tr>
<tr>
<td></td>
<td>27 $\Rightarrow$ 23</td>
<td>0.071</td>
<td>0.060</td>
<td>79.53</td>
<td>9.74</td>
<td>406.61</td>
<td>79.94</td>
<td>11.48</td>
</tr>
<tr>
<td></td>
<td>23 $\Rightarrow$ 5</td>
<td>0.021</td>
<td>0.019</td>
<td>82.54</td>
<td>32.74</td>
<td>269.03</td>
<td>82.81</td>
<td>36.49</td>
</tr>
<tr>
<td>'6'</td>
<td>6 $\Rightarrow$ 10</td>
<td>0.016</td>
<td>0.018</td>
<td>83.19</td>
<td>42.56</td>
<td>-301.75</td>
<td>82.88</td>
<td>37.68</td>
</tr>
<tr>
<td></td>
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<td>0.072</td>
<td>79.87</td>
<td>11.16</td>
<td>-380.31</td>
<td>79.49</td>
<td>9.57</td>
</tr>
<tr>
<td></td>
<td>28 $\Rightarrow$ 25</td>
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<td>0.073</td>
<td>79.10</td>
<td>8.19</td>
<td>373.75</td>
<td>79.48</td>
<td>9.52</td>
</tr>
<tr>
<td></td>
<td>25 $\Rightarrow$ 6</td>
<td>0.015</td>
<td>0.014</td>
<td>83.32</td>
<td>44.89</td>
<td>308.31</td>
<td>83.63</td>
<td>50.84</td>
</tr>
<tr>
<td>'13'</td>
<td>13 $\Rightarrow$ 15</td>
<td>0.137</td>
<td>0.034</td>
<td>77.91</td>
<td>5.06</td>
<td>3462.39</td>
<td>81.37</td>
<td>20.46</td>
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<td>6.24</td>
</tr>
<tr>
<td></td>
<td>20 $\Rightarrow$ 31</td>
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<td>0.139</td>
<td>78.72</td>
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<td>-858.48</td>
<td>77.86</td>
<td>4.97</td>
</tr>
<tr>
<td></td>
<td>31 $\Rightarrow$ 13</td>
<td>0.057</td>
<td>0.147</td>
<td>80.08</td>
<td>12.16</td>
<td>-2340.80</td>
<td>77.74</td>
<td>4.73</td>
</tr>
<tr>
<td>'14'</td>
<td>14 $\Rightarrow$ 16</td>
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<td>0.041</td>
<td>77.47</td>
<td>4.24</td>
<td>3416.83</td>
<td>80.89</td>
<td>16.84</td>
</tr>
<tr>
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<td>16 $\Rightarrow$ 21</td>
<td>0.080</td>
<td>0.094</td>
<td>79.24</td>
<td>8.64</td>
<td>-396.58</td>
<td>78.84</td>
<td>7.36</td>
</tr>
<tr>
<td></td>
<td>21 $\Rightarrow$ 32</td>
<td>0.114</td>
<td>0.147</td>
<td>78.37</td>
<td>6.10</td>
<td>-634.11</td>
<td>77.74</td>
<td>4.72</td>
</tr>
<tr>
<td></td>
<td>32 $\Rightarrow$ 14</td>
<td>0.046</td>
<td>0.122</td>
<td>80.59</td>
<td>14.92</td>
<td>-2386.13</td>
<td>78.20</td>
<td>5.70</td>
</tr>
</tbody>
</table>

Table 3-19 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for dendrimer 232. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the left side of the table.

Lastly, to confirm that the splitting of peaks 3/4 and 5/6 in ester 232 was caused by through-space coupling, VT $^{19}$F NMR was performed to observe the change in pattern.
as temperature varied. The result, also enhanced with Lorentz-to-Gauss transformation for better clarity, is shown in Figure 3-42. It was difficult to set the Gaussian linewidth at lower temperatures and therefore the splitting could not be directly observed.

![Figure 3-42 VT $^{19}$F NMR result (470 MHz) of unsymmetrical ester 232, focusing only on the peaks with AB type splitting. Full results are available in Appendix C. Red: spectra with Lorentzian lineshape. Blue: the same spectra with Gaussian lineshape obtained by Lorentz-to-Gauss transformation. Bottom right spectrum shows the spectrum at room temperature (298 K) annotated with AB coupling constant.](image)

### Table 3-20

<table>
<thead>
<tr>
<th>Peaks 3 and 4</th>
<th>Peaks 5 and 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spectra</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>$J_{AB}$&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.5 Hz</td>
</tr>
<tr>
<td>$\Delta v_{AB}$</td>
<td>5.99 Hz</td>
</tr>
<tr>
<td>$d_{F-F}$&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.43 Å</td>
</tr>
<tr>
<td>$J_{AB}$&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.5 Hz</td>
</tr>
<tr>
<td>$\Delta v_{AB}$</td>
<td>9.79 Hz</td>
</tr>
<tr>
<td>$d_{F-F}$&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.43 Å</td>
</tr>
</tbody>
</table>

<sup>a</sup> Peaks 3/4 and 5/6 of unsymmetrical ester 232 also enhanced with Lorentz-to-Gauss transformation (red).

<sup>b</sup> The AB coupling constant value ($J_{AB}$) is also the through-space coupling constant ($^{19}SF_{F-F}$).

<sup>c</sup> $^{19}F-^{19}F$ distance calculated from Eq. (2) previously shown in Chapter 2.
Similar to the unsymmetrical dendrimers, the splitting of peaks 3/4 and 5/6 are AB-type splitting (the ∆ν/J values are 1.3 and 2.2 respectively). Information that could be obtained from the spectrum, along with the calculated $^{19}\text{F} - ^{19}\text{F}$ distance is summarised in Table 3-20. The distance calculated from Eq. (2) may not be very accurate, but it illustrates the close proximity of the $^{19}\text{F}$ nuclei involved in the through-space coupling.

### 3.9 Axial Chirality of Hexaaryl Dendrimer Monoadducts and Their Ester of Chiral Auxiliary

The monoadducts of hexaaryl dendrimers were the intermediate compounds which were isolated in order to synthesise the unsymmetrical hexaaryl dendrimers, described in Section 2.7.2. It has been discussed in that section that fluorine-containing monoadducts, particularly the ortho-substituted monoadduct, gave rise to several fluorine peaks, indicating the presence of atropisomers and therefore were subjected to $^{19}\text{F} - ^{19}\text{F}$ EXSY measurement. These monoadducts were esterified with amino acid chiral auxiliary 219 and the resulting esters were also subjected to $^{19}\text{F} - ^{19}\text{F}$ EXSY measurements.

![Hexaaryl dendrimers monoadducts and esters used as models in this study. Red and green colours indicate outer and inner regions respectively.](image)

**Figure 3-43** Hexaaryl dendrimers monoadducts and esters used as models in this study. Red and green colours indicate outer and inner regions respectively.

The fluorine-containing para-substituted and ortho-substituted monoadducts that have been synthesised were 180 and 182 (Figure 3-43 top) respectively, and their hydroxy-containing analogues 181 and 183. Due to the structural similarity between
monoadducts 180, 181, 182 and 183, only monoadducts 180 and 182 were chosen as the main compounds subjected to \(^{19}\text{F}–^{19}\text{F}\) EXSY measurements.

The hydroxy-containing analogues 182 and 183 were reacted with the amino acid chiral auxiliary 219 to form the esters (Figure 3-43 bottom). These esters were obtained in excellent yield (89\% for ester 233 and 83\% for ester 234), and were also subjected to qualitative and quantitative \(^{19}\text{F}–^{19}\text{F}\) EXSY measurements.

Atropisomer analysis and assignment were performed according to the procedure used for dendrimer analysis, detailed in the previous flowchart (Figure 3-18). The para-substituted monoadduct and its ester each possessed one chiral axis, whilst the ortho-substituted analogues possessed two chiral axes. Due to the absence of symmetry in the structures of these monoadducts, the formation of meso compounds was not possible. Because of this there was no need to perform 180° rotation of the atropisomers during the assignment process.

### 3.9.1 Axial Chirality of Para-substituted Hexaaryl Dendrimer Monoadduct and Its Ester

The \(^{19}\text{F}\) peaks of para-substituted monoadducts have previously been assigned in Section 2.7.2 in Chapter 2 but further analyses of these atropisomers were conducted. The \(^{19}\text{F}–^{19}\text{F}\) EXSY spectrum of monoadduct 180 did not show correlation between the two \(^{19}\text{F}\) peaks because fluorine in the outer region does not interconvert with the fluorine in the inner region (Figure 3-44).

![Figure 3-44](image_url) The structure of monoadduct 180 showing how outer and inner regions would not interconvert due to being in different regions. Red and green colours indicate outer and inner regions respectively.

Even though the \(^{19}\text{F}\) NMR spectrum of 180 did not indicate atropisomerism, the fact that a chiral axis existed in the structure suggested that the atropisomers were present
but indistinguishable. To enable spectroscopic observation of atropisomers, the hydroxy-containing analogue (181) was esterified with amino acid chiral auxiliary 219 to form ester 233. The resulting $^{19}$F NMR spectrum of this ester (Figure 3-45) showed that the two peaks that belong to the outer region overlapped as indicated by comparison of integration values between the peaks.

![Figure 3-45 $^{19}$F NMR spectrum (470 MHz) of monoadduct ester 233. A part of the spectrum where no peak appears is cut off to achieve better clarity of the splitting of the inner region peaks. (▲ = outer region; ▶ = inner region)](image)

Without the presence of chiral auxiliary, both atropisomers above would exist as a pair of atropoenantiomers. Attachment of the chiral auxiliary has converted them into two atropodiastereomers and enabled spectroscopic observation. The possible atropisomers of the ester and their respective stereochemical configuration are shown in Figure 3-46.

![Figure 3-46 Atropisomers and their configurations in para-substituted monoadduct ester. Blue indicates chiral auxiliary. Red and green colours indicate outer and inner regions respectively.](image)

The $^{19}$F–$^{19}$F EXSY spectrum of the ester showed that the cross peaks between the two outer-region peaks were obscured and unresolvable, even with $^1$H-decoupling. Nevertheless, the evidence of interconversion between the two atropisomers could be seen with the inner-region peaks (Figure 3-47). Unfortunately, atropisomer assignment
could not be performed for this ester because of the lack of supporting data for assignment.

Figure 3-47 2D $^1$H-decoupled $^{19}$F–$^{19}$F EXSY spectrum (470 MHz) of ester 233. Bottom right inset shows the enlargement for the correlation of the outer region peaks and the overall correlation between the $^{19}$F peaks. Red and green indicate outer and inner regions respectively. (F2 = F1 = $^{19}$F NMR)

Quantitative analysis of the EXSY spectrum of the ester was performed by relying on the outer-region cross peaks. The analysis was performed on the EXSY spectrum recorded at 298 K and mixing time 0.40 s (Table 3-21).

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G^\circ_f$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$\Delta G^\circ_r$ (J mol$^{-1}$)</th>
<th>$\Delta G^\circ_r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a ≠ b (3 ≠ 4)</td>
<td>0.254</td>
<td>0.259</td>
<td>76.38</td>
<td>2.73</td>
<td>-47.70</td>
<td>76.33</td>
<td>2.67</td>
</tr>
</tbody>
</table>

Table 3-21 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for ester 233. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

3.9.2 Axial Chirality of Ortho-substituted Hexaaryl Dendrimer Monoadduct and Its Ester

In contrast to the para-substituted monoadduct, the $^{19}$F NMR spectrum of ortho-substituted monoadduct 182 showed clear indication of atropisomerism, (Figure 2-40 in
Chapter 2). 2D $^{19}$F--$^{19}$F EXSY was employed in order to study the atropisomers of this monoadduct (Figure 3-48).

![2D $^{19}$F--$^{19}$F EXSY spectrum](image)

**Figure 3-48** 2D $^{19}$F--$^{19}$F EXSY spectrum (470 MHz) of monoadduct 182. Red and green represent outer and inner regions respectively. ($F_2 = F_1 = ^{19}$F NMR)

The $^{19}$F--$^{19}$F EXSY spectrum showed correlations between the two inner-region $^{19}$F peaks and the two outer-region $^{19}$F peaks. However, as with the para-substituted analogue, there is no correlation between the peaks in the inner and outer regions.

Since one species must possess one inner-region and one outer-region peaks, EXSY result suggested the presence of two distinguishable species. The overall correlation after pairing the peaks is shown in Scheme 3-17.

![Scheme 3-17](image)

**Scheme 3-17** Atropisomer $^{19}$F peaks assignment of dendrimer 182. Red and green represent outer- and inner-region peaks respectively.

All of the possible conformations of monoadduct 182, along with their atropisomer configuration and atropisomer relations are summarised in Table 3-22 below.
Axial Chirality and Conformational Studies

<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>Atropisomer Relationship to other Atropisomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Atropoenantiomer of c</td>
</tr>
<tr>
<td></td>
<td>Atropodiastereomer of b and d</td>
</tr>
<tr>
<td></td>
<td>Atropoenantiomer of a and c</td>
</tr>
<tr>
<td>b</td>
<td>Atropodiastereomer of b and d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Atropisomer</th>
<th>Atropisomer Relationship to other Atropisomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>c</td>
<td>Atropoenantiomer of a</td>
</tr>
<tr>
<td></td>
<td>Atropodiastereomer of b and d</td>
</tr>
<tr>
<td>d</td>
<td>Atropodiastereomer of b and d</td>
</tr>
</tbody>
</table>

Table 3-22 Atropisomer conformations, configurations and relationship to other atropisomers in monoadduct 182. Red and green colours indicate outer and inner regions respectively.

Determination of the total number of distinguishable species was performed by analysing the atropisomer relations obtained from Table 3-22.

- The position of the chiral axes makes the formation of meso compounds not possible, since these atropisomers are not symmetrical.
- Atropisomers that are pairs of atropoenantiomers and therefore indistinguishable in NMR:
  - Atropisomers a and c: one species.
  - Atropisomers b and d: one species.
- As a whole, atropisomers a and b are atropodiastereomers of atropisomers c and d and therefore distinguishable in NMR: two species.
- Total number of distinguishable species in dendrimer 182: two species.

Determination of the total number of distinguishable peaks was performed by analysing the atropisomer structure in Table 3-22.

- There is no plane or axis of symmetry in any atropisomers.
- Atropisomers a and c (one species) give rise to two indistinguishable peaks, one peak each for the outer- and inner-region fluorines.
- Atropisomers b and d (one species) give rise to two indistinguishable peaks, one peak each for the outer- and inner-region fluorines.
- As a whole, atropisomers a and c are atropodiastereomers of atropisomers b and d and therefore give rise to four distinguishable peaks.
- Total number of distinguishable peaks: four peaks.
Scheme 3-18 Atropisomer arm movements in monoadduct 182. Red and green indicate fluorines and processes associated with outer and inner regions respectively. This scheme also serves as the dendrimer arm simulation.
As previously discussed with respect to ortho-substituted symmetrical dendrimer 171, computational calculation revealed the restricted rotation of 2-fluorobenzene rings (G/G’-rings). Such reasoning can also be applied to ortho-substituted monoadduct 182, but the $^{19}$F–$^{19}$F EXSY spectrum of it showed the inner-region peaks exchanging with each other, even though the rotation of fluorobenzene ring is restricted. This can be explained by the fact that rotation of the other chiral axis can also result in another atropisomer (Scheme 3-18).

The rotation of the outer ring of atropisomer a results in d. If the fluorobenzene ring could rotate, then a would result in b. However, since b and d are atropoenantiomers of each other, NMR was not able to distinguish between them. Therefore, the $^{19}$F–$^{19}$F EXSY spectrum would be consistent with the apparent rotation of fluorobenzene ring in a to form b, when in fact d was formed instead, giving rise to the correlation with the inner region.

The same reasoning also applies to the pair of atropoenantiomers (c/d) of this monoadduct, as described in Scheme 3-18. Taking these into account, the overall correlation among the atropisomers is summarised in Scheme 3-19 below.

Quantitative analysis of the EXSY spectrum of monoadduct 182 was performed using the EXSY spectrum recorded at 298 K and mixing time 0.40 s, between the two exchanging species as summarised in Table 3-23.
Axial Chirality and Conformational Studies

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-(f)}$ (s)</th>
<th>$\Delta G_r^r$ (J mol$^{-1}$)</th>
<th>$\Delta G_f^r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-(r)}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1/3 \neq 2/4$</td>
<td>0.253</td>
<td>0.213</td>
<td>76.39</td>
<td>2.74</td>
<td>425.33</td>
<td>76.81</td>
<td>3.25</td>
</tr>
</tbody>
</table>

Table 3-23 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for monoadduct 182. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

Atropisomer assignment could not be achieved due to the lack of other supporting data. Computational analysis of the monoadducts ought to be performed in the future to predict which of the pairs of enantiomers has lowest energy so that it can be compared to the results obtained from quantitative analysis.

In order to observe all of the possible atropisomers in monoadduct 182 without being obscured by pairs of enantiomers, the hydroxy-analogue of the monoadduct (183) was reacted with amino acid auxiliary 219 to form ester 234. Similar to the para-substituted monoadducts, this treatment converted the pairs of enantiomers into diastereomers and therefore enabled spectroscopic observation. The $^{19}$F NMR of the resulting ester is shown in Figure 3-49.

![Figure 3-49](image-url)

Figure 3-49 $^{19}$F NMR spectrum (470 MHz) of monoadduct ester 234. A part of the spectrum where no peak appears is omitted to achieve better clarity of the splitting of the outer region peaks. (▲ = outer region; ▲ = inner region)

The first peak in the outer region consists of two overlapping peaks. This was suggested after comparing the integration of this peak with the rest of the peaks and supported by the 2D $^1$H-decoupled $^{19}$F–$^{19}$F EXSY experiment (Figure 3-50).
The arm movement simulation (Figure 3-51) of the monoadduct ester reveals similar result to its precursor and analogue, 234 and 182, respectively. Owing to the attachment of chiral auxiliary, the pairs of atropoenantiomers have now become atropodiastereomers and therefore are distinguishable from each other.

Since each species is an atropodiastereomer of the others, all four species should theoretically be spectroscopically observable. Each species gives rise to one $^{19}\text{F}$ peak in the outer region and one in the inner region. As previously shown, eight $^{19}\text{F}$ peaks were observed in the $^{19}\text{F}$ NMR spectrum (Figure 3-49); four $^{19}\text{F}$ peaks for each region.

The arm simulation of this ester is analogous to that previously illustrated in Scheme

![Figure 3-50](image)

**Figure 3-50** 2D $^1\text{H}$-decoupled $^{19}\text{F}$–$^{19}\text{F}$ EXSY spectrum (470 MHz) of monoadduct ester 234. Bottom right inset shows the enlargement for the correlation of the outer region peaks. Top left inset shows the correlation between the peaks in each region. Red and green colours represent outer and inner regions respectively.

**Figure 3-51** Atropisomer conformations and configurations of monoadduct ester 234. Each atropisomer is atropodiastereomer of the rest. Blue, red and green colours represent the amino acid chiral auxiliary and fluorines in the outer and inner region respectively.
3-18 for monoadduct 182. The inner fluorobenzene ring in this ester is also incapable of free rotation, due to the position of the fluorine on the ring restricting the rotation.

Scheme 3-20 Atropisomer correlation in ester 234. (a) Correlation suggested from the result of $^{19}$F–$^{19}$F EXSY; (b) Correlation of what actually happened after taking into account the fact that the rotation of fluorobenzene is restricted. Red and green arrows indicate the rotation of the outer- and inner-region rings respectively.

Quantitative analysis of the EXSY spectrum of ester 234 was also performed using a spectrum recorded at 298 K and mixing time 0.40 s, between each pair of exchanging peaks as summarised in Table 3-24. Due to overlap of the first peak, it was difficult to unambiguously determine the exact value of population for each individual peak that made up the first peak and consequently making it difficult to determine the pairs of outer- and inner-region peaks overall. As a result, the values of rate constants and $\Delta G^\circ$ obtained from quantitative analysis were of each pair exchanging inner-region peaks instead of species.

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G^\circ_f$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(f)}$ (s)</th>
<th>$\Delta G_r$ (J mol$^{-1}$)</th>
<th>$\Delta G^\circ_r$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(r)}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 $\leftrightarrow$ 7</td>
<td>0.257</td>
<td>0.229</td>
<td>76.35</td>
<td>2.70</td>
<td>291.04</td>
<td>76.64</td>
<td>3.03</td>
</tr>
<tr>
<td>6 $\leftrightarrow$ 8</td>
<td>0.248</td>
<td>0.226</td>
<td>76.44</td>
<td>2.80</td>
<td>223.45</td>
<td>76.67</td>
<td>3.06</td>
</tr>
</tbody>
</table>

Table 3-24 Results obtained from quantitative analysis of the EXSY spectrum at 298 K and mixing time 0.40 s for monoadduct 234. The subscripts ‘f’ and ‘r’ respectively refer to the forward and reverse processes of the exchange systems shown on the leftmost side of the table.

In conclusion, the pentaaryl and hexaaryl dendrimers as well as their monoadducts have been subjected to spectroscopic study to reveal kinetic and thermodynamic parameters. The study confirmed that the rotation of dendrimer arms in pentaaryl dendrimers were too fast for spectroscopic observation and physical separation. In hexaaryl dendrimers, although rotation is slowed by rings G/G’ and spectroscopic observation was enabled, it was not sufficient to enable physical separation.
4 Dendrimer Expansions and Other Work

4.1 Introduction

One of the objectives of this research was to synthesise new types of polyarene dendrimers capable of focal and peripheral expansions. It was proposed that the expansions could be performed using methods other than Diels-Alder cycloaddition. The dendrimers synthesised thus far (both pentaaryl and hexaaryl) possess reactive sites that are expected to be capable of expansion; to demonstrate this, dendrimers were subjected to focal and peripheral expansion attempts. This chapter discusses these expansion attempts, the problems encountered and resulting further works.

4.2 Focal Expansions

Focal expansions can be performed on the dendrimers that possess a core hydroxy group. It has been shown during chiral resolution attempts of atropisomers (Sections 3.6 and 3.8) that esterification of the hydroxy group with both amino acid and camphorsulfonic chloride auxiliaries could be performed without any difficulties. This indicated that focal expansions could be performed through (but not limited to) esterifications with carboxylic acid branching units. Expansion can also be performed through etherification or alternatively, following conversion of hydroxy to triflate, various cross-coupling reactions (e.g. Ag/Pd-catalysed decarboxylative coupling,146 Pd-catalysed Suzuki, Stille and Sonogashira coupling reactions).

The Ag/Pd-catalysed decarboxylative coupling and other Pd-catalysed couplings could be used to obtain a dendrimer that is fully composed of aromatic rings. There is a risk of undesired peripheral expansions however, since the peripheral moieties (particularly those with bromo groups) are also able to undergo coupling reactions. The coupling methods are only viable if the peripheral groups are inert towards the reactions, (e.g. alkyl, alkoxy or nitro). These dendrimers could be obtained using CPD derivatives that possess such functionalities. Some of these CPD derivatives have also been developed by the members of our group.

Alternatively, esterification is a straightforward reaction that was used to synthesise several dendrimers (both pentaaryl and hexaaryl dendrimers) containing chiral auxiliaries. The carboxylic acid can be various aliphatic, aromatic (e.g. substituted...
benzoic acid) or combination of the two (e.g. substituted phenylacetic acid, phenylpropionic acid and cinnamic acid), therefore the resulting expanded polyarene dendrimers may possess linkers of various length and type. Since esterification is capable of opening new options for polyarene dendrimer growth, it was considered more viable than coupling reactions.

5-Bromovaleric acid (235) was attached to dendrimers Penta-OH-Br-Br (153) and Penta-OH-F-F (154) via Steglich esterification (Table 4-1).

![Dendrimer Expansions](image)

<table>
<thead>
<tr>
<th>Compd No.</th>
<th>Rings D/E/D'/E' (R°)</th>
<th>Name</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>236</td>
<td>Br</td>
<td>Penta-OVal-Br-Br</td>
<td>63</td>
</tr>
<tr>
<td>237</td>
<td>F</td>
<td>Penta-OVal-F-F</td>
<td>66</td>
</tr>
</tbody>
</table>

**Table 4-1** Attachment of 5-bromovaleric acid (235) as an aliphatic expansion unit.

The reactive alkyl bromine on 5-bromovalerate is capable of further expansion, such as alkylation or amination. The resulting dendrimers 236 and 237 can be expanded with various branching units, aliphatic or aromatic, and even with higher generation dendrimers such as PAMAM. While it was initially planned to expand these dendrimers with ethylenediamine (14) (one of the building blocks of PAMAM dendrimers), synthesis was not performed due to time constraint.

### 4.3 Peripheral Expansions

Dendrimers that possess peripheral bromine groups are capable of peripheral expansion through Pd-catalysed coupling reactions. Some of the dendrimers that were synthesised possess fluorine on their periphery, and although fluorobenzene is usually unreactive, it is capable of undergoing Suzuki cross-coupling using heterogeneous Pd catalysts.¹⁴⁷

Dendrimer Hexa-H-Phenyl-Br-Br (159) was subjected to Pd-catalysed Sonogashira coupling reaction with expansion units. These units, also referred to as ‘pendants’, possess structures that resemble the branching units of the dendrimer...
(hexaphenylbenzene) and an alkyne group as the attachment site (Figure 4-1). Similar expansion method has previously been reported for dendrimers consisting phenylene-ethylene units\textsuperscript{13,148,149} however, this has not yet been reported for polyarene dendrimers.

\textbf{Figure 4-1} A hexaphenylbenzene pendant.

The initial proposal was to expand such that the resulting expanded dendrimer has a structure that resembles the initial core 127 (blue in Scheme 4-1). Reaction of the ‘outer’ alkynes with Br-CPD 142 would result in pendant-bearing dendrimer 240. The peripheral bromines could undergo further Sonogashira and Diels-Alder reactions to afford higher generation dendrimers. This was discontinued because the CPD might also undergo Diels-Alder with the ‘inner’ alkynes.

\textbf{Scheme 4-1} Initial synthetic route for peripheral expansion.
Although the initial proposal was abandoned, the method of dendrimer expansion was still attempted. Using a different approach and pendant, the expansion attempt was performed (Scheme 4-2). A pendant with peripheral fluorines (241) was chosen, as it does not interfere with Sonogashira coupling.

Pendant 241 is not commercially available and required synthesis (Scheme 4-3). In order to obtain the hexaphenylbenzene structure while still maintaining the alkyne functionality, it was crucial for the alkyne to be introduced following the Diels-Alder reaction that formed the hexaphenylbenzene moiety. This means a phenylacetylene moiety has to be introduced to one side of the core while the other side remains unreacted (245) prior to Diels-Alder.
3-Bromoiodobenzene (243) was chosen as the starting material as the difference in reactivity between the two halides allowed for chemoselective attachment of the alkyne to afford core 245. To avoid the usage of expensive Pd catalyst in the early stage of synthesis, an alternative method was considered.

Mao and co-workers reported that phenylpropionic acid (244) could be coupled with an aryl halide through a decarboxylative coupling process catalysed by Cu(I) in DMSO. The same group also found that the reaction could be carried out in water.

Using CuI, PPh₃ and K₂CO₃, the authors demonstrated that iodo group from the aryl halide compound is chemoselectively coupled over bromo functionality. Addition of sodium iodide and tetrabutylammonium bromide is needed to carry out a coupling with the less reactive bromo group; therefore, the absence of these reagents ensures the selectivity of the reaction. Additionally, this method does not employ terminal alkynes as the alkyne source, eliminating the possible formation of homocoupling by-products. The catalytic cycle proposed by the authors is shown in Scheme 4-4.

DMSO and water were each used as solvent twice in the coupling reaction. It was found that the reaction in DMSO did not give any product in both attempts while in water 20-49% yield was obtained. It was observed that phenylpropionic acid was insoluble in DMSO, whilst 3-bromoiodobenzene was soluble. The opposite was observed when water was used as a solvent (Table 4-2). The solubility of the starting materials is thought to have played a role but was not further investigated in this thesis.
Table 4-2 Different choice of solvents affected the reaction revealed in this research.

<table>
<thead>
<tr>
<th>Solvents</th>
<th>Starting materials solubility</th>
<th>Product yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>Soluble</td>
<td>Not soluble</td>
</tr>
<tr>
<td>Water</td>
<td>Not soluble</td>
<td>Soluble</td>
</tr>
</tbody>
</table>

The Diels-Alder reaction of core 245 with F-CPD 143 was straightforward, generating excellent yield (92%). Introduction of protected alkyne functionality to the pendant was carried out via Pd-catalysed Sonogashira coupling of pendant 246 with TIPS-acetylene, affording pendant 247 in 73% yield. The final step required to obtain pendant 241 was the generation of terminal alkyne via desilylation. This was carried out using TBAF, affording pendant 241 in 95% yield.

The attachment of this pendant to dendrimer 159 was performed through Sonogashira coupling. TLC analysis indicated the presence of unreacted pendant and five other products with $R_f$ very close to each other; four could be individually isolated (the third and fourth spots could not be separated despite multiple attempts through preparative TLC). The first spot was determined to be unreacted dendrimer 159. Solubility issues of the second spot, inseparability of the third and fourth spots as well as minimal sample for the third/fourth and fifth spots meant NMR analysis was implausible. Identification of formed compounds was made via mass spectrometry (Table 4-3).

Table 4-3 Results for the synthesis of pendant-bearing dendrimer.

<table>
<thead>
<tr>
<th>Spots</th>
<th>Mass Observed</th>
<th>Molecular Formula</th>
<th>Products</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>1187 [M+H]</td>
<td>C$<em>{55}$H$</em>{34}$F$_4$</td>
<td>Homocoupled pendant (248)</td>
<td>15</td>
</tr>
<tr>
<td>III and IV</td>
<td>1820 [M]+</td>
<td>C$<em>{123}$H$</em>{77}$Br$_3$F$_2$</td>
<td>One pendant attached (249)</td>
<td>26</td>
</tr>
<tr>
<td>V</td>
<td>2333 [M]+</td>
<td>C$<em>{166}$H$</em>{104}$Br$_2$F$_4$</td>
<td>Two pendants attached (250)</td>
<td>8</td>
</tr>
</tbody>
</table>

The products formed during the expansion attempt are shown in Figure 4-2. It was not possible to determine where the pendant had attached in the dendrimer with one and two pendants without NMR analysis. Unfortunately, the NMR spectra were uninformative, but analysis of mass spectrometry allowed for the proposal of likely generated structures (Figure 4-2). Although full pendant attachment was not achieved and optimisation still has to be performed, this attempt has shown that the peripheral expansion through Sonogashira coupling could be achieved.
Figure 4-2 Possible products formed during peripheral expansion attempt.

Scheme 4-5 Alternative approach to peripheral expansions.
The optimisation of this method was not performed because dendrimer 242 could not be expanded further. Instead, using the information obtained from the first attempt, a different approach to peripheral expansion was devised (Scheme 4-5). Coupling of alkyne-terminated dendrimer 251 with fluorine-terminated pendant 253 would afford dendrimer 255, not obtained during the first attempt. Furthermore if TIPS-protected 254 was used, it would result in the formation of TIPS-terminated dendrimer 255, which, following desilylation, would be capable of further Sonogashira coupling with 254. Moreover, various works by Müllen and co-workers\textsuperscript{29,32,42,54,60,61,65,88} have shown that TIPS-terminated dendrimers do not take part during the Diels-Alder cycloaddition reaction. Therefore, this route was considered a promising possible alternative to the first route.

To realise this route, it was necessary to synthesise TIPS-terminated CPD 56 and pendants 253 and 254 (Scheme 4-6).

Core 258 is able to undergo Diels-Alder cycloaddition reactions with CPDs 143 and 56 to form pendants 253 and 254, respectively (Scheme 4-7).
Synthesis and purification of TIPS-terminated CPD 56 was found to be problematic. The initial synthesis utilised KOH as the base, but resulted in the formation of by-products likely originating from TIPS-deprotection of alkyne both from benzil 259 and CPD 56. Using tetrabutylammonium hydroxide as base and tert-butanol as solvent was reported to aid solubility of starting materials and prevent side reactions, hence this method was pursued. Purification proved to be a challenge: flash column chromatography failed to separate all of the impurities, whilst HPLC showed several peaks very close to each other.

Optimisation of synthesis and purification methods and further reactions could not be performed due to time constraint. However, because TIPS-terminated CPD has been used for dendrimer expansion in several reports, and because similar expansion approach through Sonogashira coupling has also been reported, future work should be put towards optimisation of this route.

![Figure 4-3](image)

**Figure 4-3** Proposed small graphene pendant made from hexa-peri-hexabenzocoronene (HBC) derivative. Alkyl chain is needed to improve the solubility of HBCs.

Finally, the pendant of the dendrimers is not limited only to hexaphenylbenzene moieties. It would be interesting to synthesise and characterise small graphene pendants, such as the one proposed in Figure 4-3. Using the Sonogashira coupling method to attach HBC pendants to the dendrimers would result in new polygraphene dendrimers – a new type of dendrimer that has not yet been reported.

### 4.4 Other Work

#### 4.4.1 Restricting the Rotation of Pyridyl-containing Dendrimers

Previously shown in Figure 2-21 and Figure 2-22 in Chapter 2, the $^1$H and $^{13}$C NMR spectra of the pyridyl containing dendrimer Hexa-H-(2-Pyridyl)-Br-Br 165 were not
informative due to the presence of various stereoisomers. This complication was also observed in the $^1$H and $^{13}$C NMR spectra of Hexa-OMET-(2-Pyridyl)-Br-Br (166) and Hexa-H-(2-Pyridyl)-Br-Br (167). The ortho-fluorinated dendrimers (171, 172 and 173) were initially synthesised to investigate this because it was thought that fluorine would not have a major impact on arm rotation. However, as shown previously (Figure 2-34), the $^1$H NMR spectrum of dendrimer 171 (Hexa-H-(2-Fluorophenyl)-Br-Br) was more well-defined and resolved than pyridyl-containing 165.

The main difference between 165 and 171 is the substituents that make up rings G/G’. Computational modelling showed that the fluorobenzene rings on dendrimer 171 were unable to rotate due to the electronegativity of fluorine. Therefore, it was proposed that the line broadening of the peaks in the $^1$H NMR spectrum of dendrimer 165 likely stemmed from the interconversion of atrotisomers via pyridyl-ring rotations.

In an attempt to slow the rotation of pyridyl rings, Cu(I) was introduced to generate a copper ion that was expected to form a complex with dendrimer 165 in a (1:1) ratio. This was performed by stirring reagents overnight at room temperature. The crude $^1$H and $^{13}$C NMR spectra of the resulting mixture were compared with those of dendrimer 165 (Figure 4-4).

![Figure 4-4](image)

Figure 4-4 Crude NMR spectra of the resulting mixture (top spectra) compared with pyridyl-containing dendrimer 165 (bottom spectra). (a) $^1$H NMR (400 MHz, CDCl$_3$); (b) $^{13}$C NMR (100 MHz, CDCl$_3$).
The comparison of NMR spectra clearly shows that the resulting mixture has more defined spectra than the dendrimer starting material. This suggests that the rotation of the pyridyl rings has been affected by the presence of Cu(I) ion. Whether or not the dendrimer formed a complex with the Cu(I) ion via the pyridyl rings was not investigated in this thesis. Future work should be put towards establishing this matter, as well as studying the effect of other metal ions on the dendrimer.

The mixture was also subjected to mass spectrometry analysis. The resulting spectra showed $m/z$ 1308, 1370 and 2683 (Appendix A). The first set of peaks at ~1308 (low intensity) was dendrimer 165. The set of peaks at 1370 may correspond either to $[\text{M+Cu}]^+$ species from dendrimer 165 or $[\text{M-I}]^+$ species from Cu(I) complex with one molecule of 165 (complex 261 in Scheme 4-8). A set of low intensity peaks at ~2683 may have originated from $[\text{M-I}]^+$ species from Cu(I) complex with two molecules of 165 (complex 262 in Scheme 4-8). Similar profile in the mass spectrum was obtained when the amount of ligand was doubled and reaction time was prolonged. This suggests that the formation of Cu(I) complex with dendrimer 165 was plausible.

![Scheme 4-8](image)

Scheme 4-8 Possible formation of complexes between dendrimer 165 and CuI according to mass spectrometry results.

Addition of Cu(I) has affected the NMR spectra of the resulting mixture, indicating the Cu(I) ion has interfered with the pyridyl ring rotations. Even though results from mass spectrometry suggested the possible formation of complex, it was not established for sure that the complex had been formed.
4.4.2 Synthesis of First Generation Glycodendrimer

There are numerous important biological processes that stem from the interaction between proteins and carbohydrates. These include pathogenic infections, regulation of physiological functions, as well as cellular adhesion and recognition.\textsuperscript{152} Although the individual interactions between carbohydrates and proteins are very weak, simultaneous interactions can strengthen the binding affinity between the two species.\textsuperscript{153,154} This effect is known as the ‘glycoside cluster effect’ or ‘multivalency effect’.\textsuperscript{154}

Multivalent carbohydrates may occur naturally or may be made through chemical synthesis. Man-made multivalent carbohydrates may exist as dendrimers, which are known as glycodendrimers.\textsuperscript{65,152,155,156} Multivalent carbohydrates have been applied for anti-pathogenic agents,\textsuperscript{153} biofilm inhibitors against bacterial infections,\textsuperscript{156} inhibitor against cholera toxins\textsuperscript{157,158} and many other applications. Glycodendrimers with aromatic scaffolds have been applied in nanomedicines such as drug delivery, imaging, biosensors, vaccines, anti-adhesins and nanomaterials.\textsuperscript{155}

Scheme 4-9 shows the synthesis of monovalent glycodendrimer 265 that was performed in this research, as a potential precursor for higher generation multivalent glycodendrimers. Using core 108 (provided by the author) and peracylated lactose (263), G. Potter has managed to synthesise monovalent product (264) through ‘click’ reaction. The author then used the monovalent product to conduct Diels-Alder cycloaddition with Br-CPD 142 to afford the monovalent unsymmetrical glycodendrimer (265). NMR spectroscopy proved that the lactose moiety survived the high Diels-Alder temperatures.

\begin{center}
\textbf{Scheme 4-9} Synthesis of glycodendrimer 265.
\end{center}
Similar to the other hydroxy-containing polyarene dendrimers that have been synthesised thus far, glycodendrimer (265) is capable of focal expansions following MEM-deprotection. It is also capable of peripheral expansions through the bromine groups or the sugar moiety following acetate deprotection. Other sugar moieties, ranging from mono-, di-, tri- or oligosaccharides, can also be used. Selectively-protected sugars can also be used, so that following selective deprotection, a free hydroxy is obtained and the sugar moiety is able to undergo expansion or to become a glycosyl acceptor.

The unsymmetrical glycodendrimer 265 serves as an example of how an unsymmetrical dendrimer can have entirely different properties on each side. Extrapolating this to the higher generation dendrimers, one side of the dendrimer could possess multivalent carbohydrates, whilst the other side could contain other functional groups. Therefore, the whole dendrimer would be capable of different interactions in various environments.
5 Conclusion and Future Work

5.1 Conclusion

Two types of new polyarene dendrimers with pentaaryl and hexaaryl branching units have been successfully synthesised. Both symmetrical and unsymmetrical analogues of these dendrimers were successfully obtained. The lack of symmetry was achieved during dendrimer growth by introducing CPD at different stages during the synthesis. NMR spectroscopy showed that the difference in peripheral groups in unsymmetrical dendrimer affected most parts of the dendrimer, even those that were far away from the peripheral group. Moreover, all of these dendrimers were functionalised both at the focal and peripheral regions, enabling expansion through these reactive points. All of these were achieved by synthesising cores containing functional groups that are inert towards Diels-Alder reaction.

Pentaaryl dendrimers are a group of dendrimers that contains pentaaryl branching units. Atropisomers were characterised in the solid state, but in solution the rotation of dendrimer arms were too fast for spectroscopic observation and physical separation. Attachment of chiral auxiliaries enabled spectroscopic observation and conformational study via VT $^{13}$C NMR.

Hexaaryl dendrimers are a group of dendrimers that contain hexaaryl branching units. These dendrimers also exhibited atropisomerism, giving rise to different number of isomers depending on the position of the substituents on rings G/G’ and whether the dendrimers were symmetrical or unsymmetrical. It was found that the atropisomers were observable spectroscopically but physical separation could not be achieved. Conformational studies were performed to these dendrimers mainly via $^{19}$F–$^{19}$F EXSY, revealing the kinetic and thermodynamic parameters that governed the interconversion of dendrimer atropisomers.

Focal and peripheral expansions have been attempted. Focal expansion was attempted through esterification via hydroxy group of the dendrimers. Peripheral expansion was attempted through Pd-catalysed Sonogashira coupling reaction of the peripheral bromine groups with an expansion unit labelled as the pendants. Even though full expansion was not achieved due to time constraint, the results so far indicated that expansion was possible.
5.2 Future Work

5.2.1 Conformational Locking of Hexaaryl Dendrimers

It was shown through various NMR studies that dendrimer arms rotate and that the conformational constraint was not sufficient to restrict the rotation at ambient temperature and consequently the atropisomers could not be isolated. Therefore, attempts to restrict (lock) the rotation and separate the atropisomers should be pursued. This can be achieved by increasing the size of the substituent on the additional rings or the size of the additional ring itself. Furthermore, different sizes and fluorine-containing rings should be used so that the increase in ring size and how it affects the behaviour can be studied by $^{19}$F NMR spectroscopy (Figure 5-1).

![Various rings suggested for restriction of bond rotations in dendrimer, separation of atropisomers and conformational studies through NMR spectroscopy.](image)

Two fluorine-containing pyridyl rings should be used and compared. It has been observed in ortho-substituted dendrimers that the presence of fluorine on the ring restricts the ring rotation. Therefore, the two pyridyl rings should be able to be used to study the behaviour of pyridyl-containing dendrimers. One of these would not interfere with rotation (para) whilst the other may or may not interfere (ortho). These dendrimers should be subjected to $^{19}$F NMR and $^{19}$F–$^{19}$F EXSY for conformational studies and the results should be compared to the para-substituted, ortho-substituted and pyridyl-containing dendrimers that have been synthesised in this research.

5.2.2 Conformational Studies of Pyridyl-containing Dendrimers

The pyridyl rings on the pyridyl-containing dendrimers were thought to rotate, unlike their fluorine-containing analogues, giving rise to broad peaks in the $^1$H NMR spectra. Addition of Cu(I) ion to the solution of dendrimer 165 was shown to sharpen the peaks in $^1$H NMR, suggesting that some sort of rotation locking had taken place.

Aside from using fluorine-containing pyridyl rings described in the subsection above, the pyridyl-containing dendrimers that have been obtained so far should be subjected to
Conclusions and Future Work

VT NMR experiments. Higher temperatures should be able to increase the rate of rotation, making the $^1$H peaks sharper due to fast exchange, whilst lower temperatures should slow the pyridyl ring rotations. If the temperature is low enough to lock the rotation, the $^1$H peaks will also sharpen. The $^1$H NMR spectra at low and high temperatures should then be compared to give an insight into the behaviour of pyridyl-containing dendrimers.

5.2.3 Separation of Hexaaryl Dendrimer Atropisomers

Several EXSY experiments at lower temperatures that were performed in this research showed that cross peaks were difficult and quantitative analysis could not be performed in these samples. Nevertheless, the VT EXSY experiments have shown that the rate of interconversion decreases as temperature decreases, indicating that atropisomer interconversion does not occur at low temperatures. Attempts to separate the dendrimer atropisomers should be performed through low temperature HPLC. This attempt should be performed in parallel with conformational locking.

5.2.4 Future Expansion Attempts

Peripheral expansion attempts were only achieved partially and although the alternative expansion route was met with difficulties (during the synthesis of TIPS-terminated CPD), future works should focus on the optimisation of this route. Furthermore, various different pendants should also be used, such as the one containing small graphene structure (HBC derivative), and their properties should be studied.

Peripheral expansions can also demonstrate the advantage of having different peripheral groups in unsymmetrical dendrimers; therefore there is a need to synthesise various CPD derivatives. These have been carried out within the group by J. Mistry and J. Alkabli and thus these CPDs should be used in the synthesis of dendrimers. Combination of various CPD derivatives to obtain unsymmetrical dendrimers with various peripheral groups may lead to numerous dendrimer expansion methods and therefore results in novel dendrimer structures.
Experimental

6 Experimental

6.1 General Experimental

All solvents and reagents were used as received from the manufacturer without further purification. Dry CH$_2$Cl$_2$ and THF were obtained through subsequent distillation of the solvent over calcium hydride and storage over 3 Å molecular sieves (10% m/v for CH$_2$Cl$_2$ and 20% m/v for THF) in a sealed bottle for at least 72 h prior to usage.$^{70}$ Petroleum ether used for flash column chromatography was the low boiling petroleum ether unless otherwise stated. The progress of reactions was monitored using thin layer chromatography (TLC) analysis with 0.2 mm thick TLC plates (aluminium-backed, silica gel 60 F$_{254}$) obtained from Merck. For purification using flash column chromatography, silica gel 60 (particle size 0.035-0.070 mm) was used. For purification using preparative TLC, 20 x 20 cm plates with thickness of either 1000 and 2000 microns obtained from Analtech were used. All purifications by preparative reverse-phase HPLC were performed using Agilent Technologies 1260 Infinity system equipped with a Phenomenex Luna C18 (5 µm, 2.12 x 250 mm) column at a flow rate of 15 mL/min and 254 nm detector. The mobile phase for each purification is shown in the procedure. Melting point determinations were carried out using Stuart Scientific SMP10 apparatus and are uncorrected. $^1$H NMR and $^{13}$C NMR as well as 2D COSY, HMQC and HMBC experiments were performed using a Bruker Spectrospin 400 Ultrashield spectrometer at room temperature. $^{19}$F NMR spectra and 2D $^{19}$F–$^{19}$F EXSY measurements were performed on a Bruker Spectrospin 500 Ultrashield spectrometer or Bruker Spectrospin 400 Ultrashield spectrometer at room temperature. The $^{19}$F NMR reported are of $^1$H-decoupled $^{19}$F NMR results unless otherwise stated. Variable temperature (VT) NMR experiments were performed on a Bruker Spectrospin 500 Ultrashield spectrometer at the designated temperatures. Deuterated chloroform (chloroform-$d$, CDCl$_3$) was used as a solvent in all NMR measurements, unless otherwise stated. In VT $^{13}$C NMR experiments, deuterated DMF (DMF-$d_7$) was used as solvent, while 1,4-dioxane was used as internal standard. Chemical shifts are reported in parts per million (ppm) and coupling constants in hertz (Hz). Fluorine-containing standard was not used in $^{19}$F NMR measurements; instead, the obtained $^{19}$F chemical shifts were calibrated by back-calculating from the corrected solvent signal in $^1$H NMR. All 1D and 2D NMR spectra were processed using either iNMR or Bruker TopSpin 3.1 software. Fourier Transform Infrared (FTIR) spectra were measured using Bruker ALPHA FTIR Spectrometer. UV/Vis absorption spectra were measured using JASCO.
V-660 Spectrophotometer, fluorescence emission spectra were measured using Cary Eclipse Fluorescence Spectrophotometer. UV/Vis and fluorescence measurements were performed in \( \text{CH}_2\text{Cl}_2 \) using 1 cm square quartz cells and a resolution of 1 nm. Electrospay ionisation mass spectroscopy (ESI-MS) and atmospheric pressure chemical ionisation mass spectrometry (APCI-MS) measurements were performed using Waters SQD2, Waters Micromass Q-Tof micro or Micromass Platform II mass spectrometer. Atmospheric solids analysis probe (ASAP) and nano-electrospray ionisation (nESI) measurements were performed using Thermo Scientific LTQ Orbitrap XL mass spectrometer. Gas chromatography-mass spectrometry (GC-MS) measurements were performed using Hewlett Packard 5971 MSD mass spectrometer. Matrix-assisted laser desorption/ ionisation time of flight mass spectrometry (MALDI-TOF-MS) measurements were performed using Shimadzu Axima Confidence, Applied Biosystems Voyager DE-STR or Bruker ultraflexXtreme MALDI-TOF/TOF mass spectrometers. Lastly, accurate mass measurements were measured using Thermo Finnigan MAT95XP or Thermo Scientific LTQ Orbitrap XL mass spectrometers. The quoted MALDI-TOF results for the dendrimers are of the peak with 100% abundance. Full mass spectra and isotope distribution for all dendrimers are available in Appendix A. Some of the \(^{13}\text{C}\) NMR spectra of dendrimers were unassignable due to low S/N-ratio and the presence of inseparable atropisomers. Some of these \(^{13}\text{C}\) NMR spectra are available in Appendix G.

6.2 General Procedures

**General Procedure A. Palladium-catalysed Sonogashira coupling.**

*Terminal monoalkyne with monohalide or dihalide*

Aryl halide (1.0 equiv.), \( \text{Pd(PPh}_3\text{)}_2\text{Cl}_2 \), \( \text{PPh}_3 \) and \( \text{CuI} \) (5 mol%, 10 mol% and 10 mol% for monohalide or 10 mol%, 20 mol% and 20 mol% for dihalide) were dissolved in a degassed mixture of triethylamine/anhydrous toluene in a three-necked round bottom flask. The mixture was then stirred at room temperature (for aryl iodides) or at 50-60 °C (for aryl bromides) under nitrogen atmosphere for 5-10 min. Terminal monoalkyne (1.1 equiv. for monohalide or 2.2 equiv. for dihalide) was added slowly and the mixture was left to stir overnight under nitrogen atmosphere at room temperature (for aryl iodides) or at 90 °C (for aryl bromides). \( \text{CH}_2\text{Cl}_2 \) was added into the solution, filtered and into the filtrate was slowly added 6 \( \text{N} \) \( \text{HCl} \) and the resulting mixture was stirred. The aqueous phase was removed and the organic phase was washed with saturated \( \text{NH}_4\text{Cl} \) (x 1), water (x 2), brine (x 1), dried (\( \text{MgSO}_4 \)) and concentrated.
**Experimental**

*Terminal dialkyne with monohalide*

Aryl halide (1.0 equiv.), Pd(PPh$_3$)$_2$Cl$_2$ (5 mol%), PPh$_3$ (10 mol%) and CuI (10 mol%) were dissolved in a degassed mixture of triethylamine/anhydrous toluene in a three-necked round bottom flask. The mixture was then stirred at room temperature (for aryl iodides) or at 50-60 °C (for aryl bromides) under a nitrogen atmosphere for 5-10 min. Terminal dialkyne (0.45 equiv.) was added slowly and the mixture was left to stir overnight at room temperature (for aryl iodides) or at 90 °C (for aryl bromides) under a nitrogen atmosphere. CH$_2$Cl$_2$ was added into the solution, filtered and into the filtrate was slowly added 6 N HCl and the resulting mixture was stirred. The aqueous phase was removed and the organic phase was washed with saturated NH$_4$Cl (x 1), water (x 2), brine (x 1), dried (MgSO$_4$) and the solvent was removed under vacuum.

**General Procedure B. Deprotection of silyl group using TBAF.$^{32}$**

Silyl-protected compound was dissolved in anhydrous THF. The flask was then sealed, purged with nitrogen and stirred at room temperature. Tetrabutylammonium fluoride (1.0 M in THF, 1.2 equiv. for each silyl group to be removed) was then added into the solution and the reaction mixture was stirred at room temperature for 2 h. The solvent was then removed *in vacuo* and the residue was diluted with diethyl ether, washed successively with saturated NH$_4$Cl (x 3), water (x 2) and brine (x 1), dried (MgSO$_4$) and the solvent was removed under vacuum.

**General Procedure C. Copper-free palladium-catalysed Sonogashira coupling.$^{82}$**

Terminal dialkyne (1.0 equiv.) and aryl bromides (2.4 equiv.) were added into a reaction flask that had been charged with piperidine (4.0 equiv.), PdCl$_2$ (10 mol%), PPh$_3$ (20 mol%) in a mixture of acetone/water under nitrogen atmosphere. The reaction mixture was heated at 60 °C for 24 h. The resulting mixture was left to cool to room temperature and then extracted with diethyl ether (x 5). The organic fractions were combined, dried (MgSO$_4$) and the solvent was removed under vacuum.

**General Procedure D. Knoevenagel condensation.$^{86}$**

In a 50 mL round bottom flask, benzil derivative (1.0 equiv.) and 1,3-diphenyl-2-propanone (1.0-1.1 equiv.) were dissolved in EtOH. In a different container, potassium hydroxide (0.5-0.8 equiv.) was dissolved in EtOH. The reaction mixture was heated to reflux and the solution of potassium hydroxide was added dropwise to the reaction mixture. The reaction was run for a specified amount of time and subsequently cooled
to room temperature and then to 0 °C with the aid of an ice bath.

**General Procedure E. Diels-Alder cycloaddition.**

**Symmetrical Dendrimer**
Dialkyne (1.0 equiv.) and tetraarylcylopentadienone (3.0 equiv.) were dissolved in anhydrous ortho-xylene and the reaction vessel was sealed and purged with nitrogen. The reaction mixture was then stirred at 175-200 °C until the reaction was judged to be complete by TLC. The resulting mixture was then allowed to cool to room temperature and the solvent was removed under vacuum.

**Monoadducts**
Tetraarylcylopentadienone (1.0 equiv.) and dialkyne (1.0-1.5 equiv.) were dissolved in anhydrous ortho-xylene and the reaction vessel was sealed and purged with nitrogen. The reaction mixture was then stirred at 175-200 °C until the deep purple colour of tetraarylcylopentadienone disappeared. The resulting mixture was then allowed to cool to room temperature and the solvent was removed under vacuum.

**Unsymmetrical Dendrimer**
Monoadduct (1.0 equiv.) and tetraarylcylopentadienone (1.0-3.0 equiv.) were dissolved in anhydrous ortho-xylene and the resulting solution was sealed and purged with nitrogen. The reaction mixture was then stirred at 175-200 °C until the reaction was judged to be complete by TLC. The resulting mixture was then allowed to cool to room temperature and the solvent was removed under vacuum.

**General Procedure F. Steglich esterifications.**
Into a 5 mL round bottom flask, hydroxy-containing dendrimer/monoadduct (1.0 equiv.), carboxylic acid (1.0 equiv.) and DMAP (catalytic) were added and the mixture was stirred at 0 °C with the aid of an ice bath. DCC (1.2 equiv.) was then added into the flask and the system was sealed and purged with nitrogen. Stirring was continued for 5 min at 0 °C and then 24 h at room temperature under nitrogen atmosphere. The resulting mixture was filtered to remove the urea by-product and the filtrate was then washed successively with 0.5 N HCl (x 1), saturated NaHCO3 (x 1), water (x 1), brine (x 1) and dried (MgSO4). The solvent was then removed under vacuum.
6.3 Synthesis of Cores and Their Precursors

**Dimethyl 5-Hydroxyisophthalate (111)**

5-Hydroxy isophthalic acid (10.00 g, 55 mmol) was dissolved in MeOH (150 mL). Concentrated H₂SO₄ (5 mL) was added as catalyst and the contents were heated under reflux for 12 h. The reaction mixture was cooled and excess MeOH was removed in vacuo. The residue was dissolved in EtOAc (100 mL) and washed thoroughly with saturated NaHCO₃ (2 x 100 mL) and water (100 mL). The organic layer was dried (MgSO₄) and concentrated to afford 111 (10.97 g, 95%) as white powder.

**Melting point** = 165-166 °C (lit. 165 °C); **¹H NMR** (400 MHz, CDCl₃) δ ppm: 3.88 (s, 6H, H-8/10), 5.76 (s, 1H, OH), 7.69 (d, 1.6 Hz, 2H, H-2/6) and 8.19 (t, 1.6 Hz, 1H, H-4); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 52.6 (C-8/10), 120.9 (C-2/6), 123.1 (C-4), 132.0 (C-3/5), 156.0 (C-1) and 166.2 (C-7/9); **FTIR** (neat) ν max (cm⁻¹): 3354 (m, brd, O–H stretch), 2963 (w, sp³ C–H stretch), 1699 (s, C=O stretch), [1597, 1499 (m, Ar C=C stretch)], 1353 (s, sp³ C–H bend) and [1243, 1183 (m, C–O stretch)]; **UV/Vis** (CH₂Cl₂) λ max (nm): 318 (log ε 3.40); **Fluorescence** (CH₂Cl₂, λ exc 319 nm) λ ems (nm): 337; **ESI-MS** [M+Na]⁺ m/z = 233; **HRMS** Calcd for C₁₀H₁₀O₅Na [M+Na]⁺: 233.0426, Found: 233.0432.

Data collected matched the reported data, full NMR assignment made by the author.

**Dimethyl 5-(2-Methoxyethoxy)methoxyisophthalate (112)**

Using DIPEA as Base

Into a 100 mL round bottom flask, CH₂Cl₂ (42 mL), 111 (4.20 g, 20 mmol), and DIPEA (4.65 mL, 30 mmol) were added and then cooled to 0 °C with the aid of an ice bath. 2-Methoxyethoxymethyl chloride (MEM-Cl, 3.42 mL, 30 mmol) was then added dropwise into the flask and the system was sealed and purged with nitrogen. The reaction mixture was stirred at room temperature overnight under a nitrogen atmosphere. The resulting mixture was poured into saturated aqueous NH₄Cl (40 mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (4 x 10 mL) and all of the organic extracts were combined. The combined extracts were washed with saturated NH₄Cl (20 mL), water (20 mL), brine (2 x 20 mL), and dried (MgSO₄). The solvent was removed under reduced pressure and the crude residue was purified using flash column...
Experimental

chromatography (SiO$_2$, toluene/acetone = 30:1 to 20:1) to obtain 112 (3.05 g, 51%) as a white powder.

Using Sodium Hydride as Base

Into a 100 mL round bottom flask, NaH (60% dispersion in mineral oil, 1.80 g, 45 mmol) and dry THF (42 mL) were added. The mixture was stirred, sealed, purged with nitrogen and then cooled to 0 °C with the aid of an ice bath. 111 (4.20 g, 20 mmol) was added portion-wise over 5 min and then 2-methoxyethoxymethyl chloride (3.42 mL, 30 mmol) was also added into the flask and the system was sealed again. The reaction mixture was stirred at 0 °C overnight under a nitrogen atmosphere. Water (40 mL) was then added carefully and the layers were separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (5 x 20 mL). All of the organic extracts were combined and dried (MgSO$_4$). The solvent was removed under reduced pressure and the crude residue was purified using flash column chromatography (SiO$_2$, toluene/acetone = 25:1) to obtain 112 (5.85 g, 98%) as a white powder.

Data for both methods:

TLC R$_f$ = 0.33 (toluene/acetone = 20:1); melting point = 88-89 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 3.31 (s, 3H, H-1), 3.48-3.50 (m, 2H, H-2), 3.75-3.78 (m, 2H, H-3), 3.86 (s, 6H, H-11/12), 5.28 (d, 1.6 Hz, 2H, H-6/10) and 8.27 (t, 1.6 Hz, 1H, H-8); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 52.5 (C-12/14), 59.1 (C-1), 68.0 (C-3), 71.5 (C-2), 93.4 (C-4), 121.6 (C-6/10), 124.2 (C-8), 131.9 (C-7/9), 157.2 (C-5) and 166.0 (C-11/13); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [2998, 2957, 2895, 2814 (w, sp$^3$ C–H stretch)], 1723 (s, C=O stretch), 1592 (m, Ar C=C stretch), [1436, 1330 (m, sp$^3$ C–H bend)] and [1214, 1169, 1099 (s, C–O stretch)]; UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 304 (log $\varepsilon$ 3.48); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 316 nm) $\lambda_{\text{ems}}$ (nm): 338; ESI-MS [M+Na]$^+$ m/z = 321; HRMS Calcd for C$_{14}$H$_{18}$O$_7$Na [M+Na]$^+$: 321.0950, Found: 321.0956.

(5-((2-Methoxyethoxy)methoxy)-1,3-phenylene)dimethanol (113)$^{160}$

To a stirred suspension of LiAlH$_4$ (1.52 g, 40 mmol) in dry THF (30 mL) was added dropwise a solution of 112 (2.38 g, 8 mmol) in dry THF (16 mL) at 0 °C. After 1 h at 0 °C, the suspension was allowed to reach room temperature and stirred overnight. The reaction was quenched with saturated NH$_4$Cl solution (30 mL) and stirred vigorously for 221
30 min. The resulting mixture was subjected to filtration under vacuum and the filtrate was washed with CH$_2$Cl$_2$ (3 x 50 mL). The organic phase was washed with water (50 mL), brine (50 mL), and dried (MgSO$_4$). The solvent was removed and the residue was purified with flash column chromatography (SiO$_2$, CH$_2$Cl$_2$/MeOH = 40:1 to 30:1) to give a crystalline white solid of 113 (1.65 g, 85%).

**TLC R**$_f$ = 0.12 (CH$_2$Cl$_2$/MeOH = 15:1); **melting point** = 43-44 °C; **$^1$H NMR** (400 MHz, CDCl$_3$) δ ppm: 3.14 (t, 5.2 Hz, 2H, OH), 3.27 (s, 3H, H-1), 3.44-3.46 (m, 2H, H-2), 3.70-3.72 (m, 2H, H-3), 4.47 (d, 5.2 Hz, 4H, H-11/12), 5.15 (s, 2H, H-4), 6.83 (s, 2H, H-6/10) and 6.86 (s, 1H, H-8); **$^{13}$C NMR** (100 MHz, CDCl$_3$) δ ppm: 59.0 (C-1), 64.7 (C-11/12), 67.6 (C-3), 71.6 (C-2), 93.4 (C-4), 113.7 (C-6/10), 118.8 (C-8), 143.0 (C-7/9) and 157.4 (C-5); **FTIR** (neat) $\nu$$_{\text{max}}$ (cm$^{-1}$): 3257 (m, brd, O–H stretch), [2980, 2920, 2895, 2875, 2822 (m, sp$^3$ C–H stretch)], 1596 (m, Ar C=C stretch), [1455, 1368 (m, sp$^3$ C–H bend)], [1203, 1174, 1099 (m, C–O stretch)]; **UV/Vis** (CH$_2$Cl$_2$) $\lambda$$_{\text{max}}$ (nm): 277 (log $\varepsilon$ 3.11); Non-fluorescent; **ESI-MS** [M+H]$^+$ m/z = 265; **HRMS** Calcd for C$_{12}$H$_{18}$O$_5$Na [M+Na]$^+$: 265.1052, Found: 265.1062.

**Synthesis of Bestmann-Ohira Reagent**

4-Acetamidobenzenesulfonyl Azide (115)

Into a round bottom flask was added 4-acetamidobenzenesulfonyl chloride (10.00 g, 43 mmol) in CH$_2$Cl$_2$ (80 mL) and TBAI (40 mg). The mixture was stirred for 5 min and then a solution of NaN$_3$ (4.20 g, 66 mmol) in water (20 mL) was also added. The reaction mixture was stirred overnight at room temperature. The organic layer that was formed was then separated from the aqueous layer, washed with water (2 x 30 mL) and dried (MgSO$_4$). The solvent was then removed under reduced pressure to obtain pale yellow crystals of 115 (8.97 g, 87%).
(w, N–H stretch), [3184, 3110 (w, Ar C–H stretch)], 2117 (s, N=N=N), 1673 (m, C=O stretch), [1584, 1527, 1497 (s, Ar C=C stretch]) and [1361, 1159 (s, S=O stretch)]; ESI-MS [M+H]^+ m/z = 242.

Data collected matched the reported data.50,73

**Dimethyl 1-Diazo-2-oxopropylphosphonate (51)**

A three-necked round bottom flask was charged with dimethyl 3-oxopropylphosphonate (2.49 g, 15 mmol) in toluene (15 mL). The solution was cooled to 0 °C, stirred under nitrogen, and then NaH (0.72 g of 60% dispersion in mineral oil, 18 mmol) was added over 10 min. After the evolution of gas had ceased, a solution of 115 (3.59 g, 15 mmol) in THF (5 mL) was added dropwise over 10 min. The reaction mixture was stirred for 16 h at room temperature under a nitrogen atmosphere. The resulting mixture was then filtered through a Celite® pad, rinsed thoroughly with Et₂O, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (SiO₂, CH₂Cl₂/MeOH = 40:1 and then SiO₂, hexane/EtOAc = 1:1) and the product-containing fractions were concentrated, separated into several flasks and left on the high vacuum line for several days to afford pure 51 (2.55 g, 88%) as a clear yellow liquid.

\[\text{H NMR (400 MHz, CDCl₃)} \delta \text{ ppm}: 2.26 (s, 3H, H-3) \text{ and } 3.84 (d, } ^3J_{H-P} = 12 \text{ Hz, 6H, H-4/5); \text{ C NMR (100 MHz, CDCl₃)} \delta \text{ ppm: } 27.2 \text{ (C-3), 53.6 (d, } ^2J_{C-P} = 5.5 \text{ Hz, C-4/5), 60.4 (C-1) and 189.9 (d, } ^2J_{C-P} = 3.1 \text{ Hz, C-2); FTIR (neat) } \nu_{\text{max}} \text{ (cm}^{-1}): [2959, 2956 (w, } sp^3 \text{ C–H stretch)], 2118 \text{ (m, C=N₂ stretch), 1655 (m, C=O stretch), 1364 (m, } sp^3 \text{ C–H bend), 1262 (s, P=O stretch) and 1179 (m, C–O stretch); ESI-MS [M+Na]^+ m/z = 215.}

Data collected matched the reported data.50

**50,73(5-((2-Methoxyethoxy)methoxy)-1,3-phenylene)dimethanal (114)**

Compound 113 (0.6050 g, 2.5 mmol) was dissolved in dry CH₂Cl₂ (20 mL) in a 50 mL round bottom flask. Activated MnO₂ (4.3500 g, 50.0 mmol, 20 equiv.) was added into the solution and the mixture was stirred at room temperature for 48 h. The progress of reaction was monitored by TLC analysis and judged to be complete after all of the starting materials had been consumed. The resulting mixture was filtered through a
Celite® pad with CH₂Cl₂ as eluent and the solvent was removed under pressure. The residue was then purified by flash column chromatography (SiO₂, CH₂Cl₂/MeOH = 40:1) to afford **114** (0.4257 g, 72%) as yellow needles.

**Dialdehyde (114) data:**

*Experimental*

![TLC diagram](image)

**TLC** R<sub>f</sub> = 0.53 (CH₂Cl₂/MeOH = 15:1); **melting point =** 52-53 °C; **¹H NMR** (400 MHz, CDCl₃) δ ppm: 3.30 (s, 3H, H-1), 3.48-3.51 (m, 2H, H-2), 3.77-3.80 (m, 2H, H-3), 5.32 (s, 2H, H-4), 7.74 (d, 1.6 Hz, 2H, H-6/10), 7.96 (t, 1.6 Hz, 1H, H-8) and 9.99 (s, 2H, H-11/12); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 59.1 (C-1), 68.2 (C-3), 71.5 (C-2), 93.6 (C-4), 122.0 (C-6/10), 124.6 (C-8), 138.4 (C-7/9), 158.5 (C-5) and 190.8 (C-11/12); **FTIR** (neat) υ<sub>max</sub> (cm⁻¹): [2986, 2931, 2907, 2851, 2827, 2741 (w, sp<sup>3</sup> C–H stretch)], 1688 (s, C=O stretch), 1591 (m, Ar C=C stretch), [1452, 1379 (m, sp<sup>3</sup> C–H bend)] and [1199, 1152, 1106 (s, C–O stretch)]; **UV/Vis** (CH₂Cl₂) λ<sub>max</sub> (nm): 323 (log ε 3.56); **Fluorescence** (CH₂Cl₂, λ<sub>exc</sub> 373 nm) λ<sub>ems</sub> (nm): 413, 438 and 463; **ESI-MS** [M+Na]<sup>+</sup> m/z = 261; **HRMS** Calcd for C₁₂H₁₄O₅Na [M+Na]<sup>+</sup>: 261.0739, Found: 261.0751.

**Monoaldehyde (121) data:**

![TLC diagram](image)

**TLC** R<sub>f</sub> = 0.45 (CH₂Cl₂/MeOH = 15:1); **¹H NMR** (400 MHz, CDCl₃) δ ppm: 2.23 (br s, 1H, OH) 3.29 (s, 3H, H-1), 3.48-3.50 (m, 2H, H-2), 3.75-3.77 (m, 2H, H-3), 4.67 (s, 2H, H-12) 5.25 (s, 2H, H-4), 7.25-7.26 (m, 1H, H-8), 7.38-7.39 (m, 1H, H-6), 7.44-7.45 (m, 1H, H-10) and 9.88 (s, 2H, H-11); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 59.0 (C-1), 64.3 (C-12), 71.5 (C-2), 93.5 (C-4), 115.6 (C-6), 120.8 (C-8), 121.7 (C-10), 137.9 (C-7), 143.8 (C-9), 158.0 (C-5) and 191.1 (C-11); **ESI-MS** [M+Na]<sup>+</sup> m/z = 263.

**1,3-Diethynyl-5-((2-methoxyethoxy)methoxy)benzene (108)**

Compound **51** (0.92 g, 4.8 mmol) was added into a solution of **114** (0.48 g, 2.0 mmol) and K₂CO₃ (0.55 g, 4.0 mmol) in anhydrous MeOH (30 mL). The reaction vessel was sealed and purged with nitrogen and then stirred for 16 h at room temperature. The resulting mixture was diluted with diethyl ether (50 mL), washed with a 5% solution of NaHCO₃ (20 mL) and dried over MgSO₄. The solvent was then removed under vacuum.
and the residue was purified by flash column chromatography (SiO₂, hexane/EtOAc = 7:3) to afford 108 (0.49 g, 44%) and monoalkyne by-product 78 (0.49 g, 44%) both as yellow liquids. (After cleaner Bestmann-Ohira reagent was obtained, 0.98 g (88%) yield of 108 was obtained.)

**Dialkyne (108) data:**

TLC R_f = 0.60 (hexane/EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl₃) δ ppm: 2.99 (s, 2H, H-12/14), 3.31 (s, 3H, H-1), 3.48-3.50 (m, 2H, H-2), 3.73-3.75 (m, 2H, H-3), 5.18 (s, 2H, H-4), 7.10 (d, 1.6 Hz, 2H, H-6/10) and 7.19 (t, 1.6 Hz, 1H, H-8); \(^{13}\)C NMR (100 MHz, CDCl₃) δ ppm: 59.1 (C-1), 67.9 (C-3), 71.5 (C-2), 77.9 (C-12/13), 82.4 (C-11/13), 93.4 (C-4), 120.5 (C-6/10), 123.5 (C-7/9), 129.4 (C-8) and 156.8 (C-5); FTIR (neat) \(\nu_{max}\) (cm\(^{-1}\)): 3289 (m, \(sp^\equiv\) C–H stretch), [2924, 2881, 2819 (m, \(sp^3\) C–H stretch), [1578, 1551 (m, Ar C=C stretch)], [1453, 1317 (m, \(sp^3\) C–H bend)] and [1200, 1131, 1099 (m, C–O stretch)]; UV/Vis (CH₂Cl₂) \(\lambda_{max}\) (nm): 247, 253, 290 and 311 (log ε 4.21, 4.09, 3.09 and 3.35); Fluorescence (CH₂Cl₂, \(\lambda_{exc}\) 316 nm) \(\lambda_{em}\) (nm): 331; ESI-MS [M+Na]\(^+\) m/z = 253; HRMS Calcd for C₁₄H₁₄O₃Na [M+Na]\(^+\): 253.0835, Found: 253.0838.

**Monoalkyne (122) data:**

TLC R_f = 0.45 (hexane/EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl₃) δ ppm: 3.08 (s, 1H, H-12), 3.31 (s, 3H, H-1), 3.48-3.50 (m, 2H, H-2), 3.73-3.77 (m, 2H, H-3), 5.25 (s, 2H, H-4), 7.36 (dd, 1.6 and 2.4 Hz, 1H, H-6), 7.48 (dd, 1.6 and 2.4 Hz, 1H, H-10), 7.56 (t, 1.6 Hz, 1H, H-8) and 9.87 (s, 1H, H-13); \(^{13}\)C NMR (100 MHz, CDCl₃) δ ppm: 59.1 (C-1), 68.1 (C-3), 71.5 (C-2), 78.7 (C-4), 82.0 (C-11), 93.5 (C-4), 116.8 (C-10), 124.3 (C-7), 125.7 (C-6), 127.4 (C-8), 137.8 (C-9), 157.6 (C-5) and 191.1 (C-13); ESI-MS [M+Na]\(^+\) m/z = 257.

**1-(tert-Butyldimethylsiloxy)-3,5-dibromobenzene (124)**

3,5-Dibromophenol (5.0400 g, 20 mmol) was dissolved in anhydrous CH₂Cl₂ (55 mL). Imidazole (2.1760 g, 32 mmol) and DMAP (0.2440 g, 2 mmol) were then added into the solution and the mixture was stirred until a clear solution was formed. The solution was then cooled to 0 °C with the aid of an ice bath and tert-butyldimethylsilyl chloride.
Experimental

(TBDMS-Cl, 3.3160 g, 22 mmol) was added. The reaction mixture was then allowed to warm to room temperature and stirred at room temperature for 16 h. The resulting mixture was filtered and the filtrate was acidified with 2% HCl (10 mL). The organic phase was separated, washed successively with saturated NH₄Cl (30 mL), saturated NaHCO₃ (30 mL), brine (30 mL) and dried (MgSO₄). The solvent was removed under vacuum and the residue was purified by flash column chromatography (SiO₂, hexane/EtOAc = 95:5) to afford 124 (6.6735 g, 91%) as colourless liquid.

\[ \text{TLC } R_f = 0.85 \text{ (hexane/EtOAc = 95:5); } \]

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{) } \delta \text{ ppm: 0.22 (s, 6H, H-5/6), 0.98 (s, 9H, H-1/2/3), 6.94 (d, 1.6 Hz, 2H, H-8/12) and 7.27 (t, 1.6 Hz, 1H, H-10); } \]

\[ \text{\textsuperscript{13}C NMR (100 MHz, CDCl}_3\text{) } \delta \text{ ppm: -4.4 (C-5/6), 18.3 (C-4), 25.7 (C-1/2/3), 122.9 (C-10), 125.5 (C-9/11), 127.3 (C-8/12) and 157.2 (C-7); } \]

\[ \text{FTIR (neat) } \nu_{\text{max}} \text{ (cm}^{-1}\text{): [3113, 3074 (w, Ar C–H stretch)], [2955, 2930, 2886, 2858 (m, } \text{sp}^3 \text{C–H stretch)], [1578, 1551 (s, Ar C=C stretch)], 1426 (s, Si–C stretch), 1362 (w, } \text{sp}^3 \text{C–H bend), 1252 (s, Si–O stretch) and 1086 (w, Ar C–Br stretch); UV/Vis (CH}_2\text{Cl}_2\text{) } \lambda_{\text{max}} \text{ (nm): 280 (log } \varepsilon \text{ 3.03); Fluorescence (CH}_2\text{Cl}_2\text{, } \lambda_{\text{exc}} \text{ 373 nm) } \lambda_{\text{ems}} \text{ (nm): 413, 438 and 465; APCI-MS [M+H] }^+ \text{ m/z = 365 (43%), 367 (100%) and 369 (43%); HRMS Calcd for C}_{12}\text{H}_{18}^{79}\text{Br}_2\text{OSi [M}^+\text{) (monoisotopic): 363.9488, Found: 363.9484.} \]

Data collected matched the reported data,\textsuperscript{161} full NMR assignment made by the author.

\[ 1-(\text{tert-Butyldimethylsilyloxy})-3,5\text{-bis}(2\text{-trimethylsilyl})\text{ethynyl})\text{benzene (125)} \]

Compound 124 (6.0902 g, 16.6 mmol, 1.0 equiv.), TMS-acetylene (5.16 mL, 36.6 mmol, 2.2 equiv.), Pd(PPh₃)₂Cl₂ (0.2336 g, 0.33 mmol, 10 mol%), PPh₃ (0.1744 g, 0.66 mmol, 20 mol%), CuI (0.1268 g, 0.66 mmol, 20 mol%), Et₃N (60 mL) and anhydrous toluene (30 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO₂, hexane) afforded product 125 (5.9905 g, 90%) and monocoupled byproduct 126 (0.2333 g, 4%) both as yellow viscous liquids.

\[ \text{Dialkyne (125) data:} \]
Experimental

TLC \( R_f = 0.30 \) (hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 0.20 (s, 6H, H-17/18), 0.24 (s, 18H, H-9/10/11/14/15/16), 0.98 (s, 9H, H-20/21/22), 6.87 (d, 1.2 Hz, 2H, H-2/6) and 7.21 (t, 1.2 Hz, 1H, H-4); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: -4.3 (C-17/18), 0.1 (C-9/10/11/14/15/16), 18.3 (C-19), 25.7 (C-20/21/22), 94.7 (C-8/13), 104.1 (C-7/12), 123.9 (C-2/6), 124.4 (C-3/5), 129.2 (C-4) and 155.3 (C-1); FTIR (neat) \( \nu_{\text{max}} \) (cm\(^{-1}\)): [2957, 2930, 2898, 2859 (m, \( sp^3 \) C–H stretch)], 2161 (w, C≡C stretch), 1575 (m, Ar C=C stretch), 1415 (m, Si–C stretch), 1328 (m, \( sp^3 \) C–H bend), 1249 (m, Si–O stretch) and 1162 (m, C–O stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \( \lambda_{\text{max}} \) (nm): 241, 260 and 317 (log \( \varepsilon \) 4.76, 4.40 and 3.30); Fluorescence (CH\(_2\)Cl\(_2\), \( \lambda_{\text{exc}} \) 316 nm) \( \lambda_{\text{em}} \) (nm): 338; APCI-MS [M+H]^+ \( m/z \) = 401 (100%), 402 (37%), 403 (16%) and 404 (4%); HRMS Calcd for C\(_{22}\)H\(_{37}\)OSi [M+H]^+: 401.2152, Found: 401.2047.

Monoalkyne (126) data:

TLC \( R_f = 0.53 \) (hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 0.20 (s, 6H, H-12/13), 0.24 (s, 9H, H-9/10/11), 0.97 (s, 9H, H-15/16/17), 6.84 (dd, 1.2 and 2.0 Hz, 1H, H-2), 6.95 (dd, 1.2 and 2.0 Hz, 1H, H-6) and 7.22 (dd, 2.0 and 1.2 Hz, 1H, H-4); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: -4.3 (C-12/13), 0.0 (C-9/10/11), 18.3 (C-14), 25.7 (C-15/16/17), 95.6 (C-8), 103.4 (C-7), 122.2 (C-5), 122.3 (C-2), 124.2 (C-6), 125.6 (C-3), 128.1 (C-4) and 156.2 (C-1); FTIR (neat) \( \nu_{\text{max}} \) (cm\(^{-1}\)): [2956, 2930, 2897, 2859 (m, \( sp^3 \) C–H stretch)], 2155 (w, C≡C stretch), [1586, 1554 (m, Ar C=C stretch)], 1422 (m, Si–C stretch), 1362 (w, \( sp^3 \) C–H bend), 1250 (m, Si–O stretch) and 1160 (m, C–O stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \( \lambda_{\text{max}} \) (nm): 253, 262 and 300 (log \( \varepsilon \) 4.21, 4.23 and 3.33); Fluorescence (CH\(_2\)Cl\(_2\), \( \lambda_{\text{exc}} \) 373 nm) \( \lambda_{\text{em}} \) (nm): 412, 437 and 465; GC/MS-EI [M]^+ \( m/z \) = 382 (80%), 383 (35%), 384 (100%) and 385 (30%); HRMS Calcd for C\(_{17}\)H\(_{27}\)O\(_7\)BrSi\(_2\) [M]^+: 382.0778, Found: 382.0768.

3,5-Diethynylphenol (109)

Through MEM Deprotection of 108 using ZnBr\(_2\)\(^{68}\)

Compound 108 (1.00 g, 4.35 mmol) and anhydrous CH\(_2\)Cl\(_2\) (300 mL) were added into a 1 L round bottom flask and stirred. Anhydrous ZnBr\(_2\) (9.80 g, 43.5 mmol, 10 equiv.) was then added into the solution and the reaction mixture was stirred at room
temperature. The reaction was judged to be complete after no more starting material was observed by TLC analysis. The resulting mixture was then washed with saturated NaHCO$_3$ (100 mL) brine (100 mL) and dried (MgSO$_4$). The residue was then purified by flash column chromatography (SiO$_2$, hexane/acetone = 6:1) to give 109 (0.18 g, 28%) as a white powder.

Through MEM Deprotection of 108 using Trifluoroacetic Acid (TFA)$^{79}$

Compound 108 (4.2820 g, 18.6 mmol) was dissolved in CH$_2$Cl$_2$ (30 mL), stirred and cooled to 0 °C with the aid of an ice bath. TFA (2.87 mL, 37.2 mmol, 2.0 equiv.) was then added dropwise into the solution and the reaction mixture was stirred at room temperature for 18 h. The resulting mixture was then washed with saturated NaHCO$_3$ (30 mL) and brine (30 mL), dried over MgSO$_4$ and concentrated. The residue was then purified twice by flash column chromatography (SiO$_2$, hexane/acetone = 8:1 to 6:1 and then SiO$_2$, hexane/Et$_2$O = 5:1) to give 109 (1.5736 g, 60%) as a white powder.

Through TBDMS Deprotection of 125

Compound 125 (2.8893 g, 7.2 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 26 mL, 26 mmol, 3.6 equiv.) and anhydrous THF (200 mL) were treated as described in General Procedure B. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 95:5) afforded 109 (0.9977 g, 97%) as a white powder.

Data for all methods:

TLC $R_f$ = 0.23 (hexane/acetone = 4:1), $R_f$ = 0.30 (hexane/Et$_2$O = 4:1) and $R_f$ = 0.23 (hexane/EtOAc = 10:1); melting point = 87-88 °C (lit. 88-89 °C) $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 3.07 (s, 2H, H-8/10), 5.02 (br s, $^1$H, OH), 6.94 (d, 1.2 Hz, 2H, H-2/6) and 7.20 (t, 1.2 Hz, $^1$H, H-4); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 78.1 (C-8/10), 82.4 (C-7/9), 119.7 (C-2/6), 123.8 (C-3/5), 128.7 (C-4) and 155.2 (C-1); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3257 (m, brd, O–H stretch and sp $\equiv$C–H stretch), [3068, 3054 (w, Ar C–H stretch)], 2106 (w, C=C stretch), [1582, 1482 (m, Ar C=C stretch)] and 1223 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 247, 253, 304 and 313 (log $\varepsilon$ 4.22, 4.04, 3.46 and 3.48); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 316 nm) $\lambda_{\text{ems}}$ (nm): 332; ESI-MS [M+H]$^+$ $m/z$ = 143; HRMS Calcd for C$_{10}$H$_7$O [M+H]$^+$: 143.0497, Found: 143.0493.

Data collected matched the reported data,$^{162}$ full NMR assignment made by the author.
Experimental

1,3-bis(Phenylethynyl)benzene (127)

Bromobenzene (0.9 mL, 8.4 mmol, 1.0 equiv.), 1,3-diethynylbenzene (0.5 mL, 3.8 mmol, 0.45 equiv.), Pd(PPh₃)₂Cl₂ (0.2949 g, 0.42 mmol, 5 mol%), PPh₃ (0.2201 g, 0.84 mmol, 10 mol%), CuI (0.1601 g, 0.84 mmol, 10 mol%), Et₃N (36 mL) and anhydrous toluene (18 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO₂, hexane) afforded 127 (0.3514 g, 33%) as a white solid.

TLC R_f = 0.24 (hexane); melting point = 113-114 °C (lit.163 111-113.5 °C); ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.33-7.40 (m, 7H, H-5/11/12/13/19/20/21), 7.50-7.52 (m, 2H, H-4/6), 7.55-7.57 (m, 4H, H-10/14/18/22) and 7.74 (dt, 1.6 and 0.4 Hz, 1H, H-2); ¹³C NMR (100 MHz, CDCl₃) δ ppm: 88.7 (C-7/15), 90.1 (C-8/16), 123.1 (C-1/3), 123.8 (C-9/17), 128.5 (C-11/13/19/21), 128.6 (C-5), 128.6 (C-12/20), 131.4 (C-4/6), 131.8 (C-10/14/18/22) and 134.7 (C-2); FTIR (neat) υ_max (cm⁻¹): [3076, 3051, 3032, 3016 (w, Ar C–H stretch)] and [1596, 1569, 1489 (m, Ar C=C stretch)]; UV/Vis (CH₂Cl₂) λ_max (nm): 273, 284 and 300 (log ε 4.68, 4.80 and 4.72); Fluorescence (CH₂Cl₂, λ_exc 316 nm) λ_em (nm): 335, 345 and 355; APCI-MS [M+H]^+ m/z = 279 (100%), 280 (22%) and 281 (2%); HRMS Calcd for C₂₂H₁₅ [M+H]^+: 279.1174, Found: 279.1164.

Data collected matched the reported data,¹⁶³ full NMR assignment made by the author.

(3,5-bis(Phenylethynyl)phenoxy)(tert-butyl)dimethyl silane (128)

Compound 124 (2.1960 g, 6 mmol, 1.0 equiv.), phenylacetylene (1.45 mL, 13.2 mmol, 2.2 equiv.), Pd(PPh₃)₂Cl₂ (0.4212 g, 0.6 mmol, 10 mol%), PPh₃ (0.2286 g, 1.2 mmol, 20 mol%), CuI (0.2286 g, 1.2 mmol, 20 mol%), Et₃N (48 mL) and anhydrous toluene (24 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO₂, petroleum ether) afforded 128 (0.7043 g, 58%) as a yellow solid.

TLC R_f = 0.18 (petroleum ether); melting point = 97-98 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: 0.26 (s, 6H, H-5/6), 1.03 (s, 9H, H-1/2/3), 7.00 (d, 1.6 Hz, 2H, H-8/12), 7.34-7.40 (m, 7H, H-10/17/18/19/25/26/27) and 7.53-7.57 (m, 4H, H-16/20/24/28); ¹³C NMR (100 MHz, CDCl₃) δ ppm: 88.7 (C-7/15), 90.1 (C-8/16), 123.1 (C-1/3), 123.8 (C-9/17), 128.5 (C-11/13/19/21), 128.6 (C-5), 128.6 (C-12/20), 131.4 (C-4/6), 131.8 (C-10/14/18/22) and 134.7 (C-2);
Experimental

1,3-bis(2-Pyridylethynyl)benzene (129)

Through Copper-free Sonogashira coupling reaction method

1,3-Diethynylbenzene (0.13 mL, 1 mmol, 1.0 equiv.), 2-bromopyridine (0.23 mL, 2.4 mmol, 2.4 equiv.), piperidine (0.39 mL, 4 mmol, 4.0 equiv.), PdCl\(_2\) (0.0180 g, 0.1 mmol, 10 mol%), PPh\(_3\) (0.1301 g, 0.5 mmol, 20 mol%) and acetone/water (3:3 g) were treated as described in General Procedure C. Purification by flash column chromatography (SiO\(_2\), hexane/EtOAc = 15:1 to 0:1) afforded 129 (0.1382 g, 49%) as a dark yellow powder.

Through conventional Sonogashira coupling reaction method

2-Iodopyridine (2.6 mL, 24 mmol, 1.0 equiv.), 1,3-diethynylbenzene (1.45 mL, 11 mmol, 0.45 equiv.), Pd(PPh\(_3\))\(_2\)Cl\(_2\) (0.8561 g, 1.2 mmol, 5 mol%), PPh\(_3\) (0.6390 g, 2.4 mmol, 10 mol%), CuI (0.4646 g, 2.4 mmol, 10 mol%), Et\(_3\)N (50 mL) and anhydrous toluene (50 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO\(_2\), CH\(_2\)Cl\(_2\)/EtOAc = 98:2 to 80:20) afforded 129 (2.2987 g, 75%) as a dark yellow powder.

Data for both methods:

TLC \( R_f \) = 0.25 (hexane/EtOAc = 1:1) and \( R_f \) = 0.10 (CH\(_2\)Cl\(_2\)/EtOAc = 20:1); melting point = 97-98 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 7.23 (\( ddd; \) 1.2, 4.9 and 7.6 Hz; 2H, H-3/20), 7.34 (\( ddd; \) 0.6, 7.7 and 8.1 Hz; 1H, H-11), 7.51 (\( dt; \) 1.2 and 7.8 Hz, 2H, H-5/18), 7.57 (\( dd; \) 1.7 and 7.7 Hz, 2H, H-10/12), 7.66 (\( td; \) 1.8 and 7.8 Hz, 2H, H-4/19), 7.80 (\( td; \) 0.6 and 1.7 Hz, 1H, H-14) and 8.60 (\( ddd; \) 1.0, 1.8 and 4.9 Hz, 2H, H-2/21); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: 88.2 (C-8/15), 230
Experimental

Data collected matched the reported data,\textsuperscript{164} full NMR assignment made by the author. No melting point data reported in the literature.

\textit{1,3-bis(2-Pyridylethynyl)-5-((2-methoxyethoxy)methoxy)benzene (130)}

Compound 108 (0.2300 g, 1.0 mmol, 1.0 equiv.), 2-bromopyridine (0.23 mL, 2.4 mmol, 2.4 equiv.), piperidine (0.39 mL, 4.0 mmol, 4.0 equiv.), PdCl\(_2\) (0.0180 g, 0.1 mmol, 10 mol%), PPh\(_3\) (0.1301 g, 0.5 mmol, 20 mol%) and acetone/water (3:3 g) were treated as described in General Procedure C. Purification by flash column chromatography (SiO\(_2\), hexane/EtOAc = 15:1 to 0:1 and SiO\(_2\), toluene/acetone = 20:1 to 5:1) afforded 130 (0.2265 g, 59%) as a yellow solid. 

\textbf{TLC} \(R_f = 0.28\) (hexane/EtOAc = 4:1) and 0.23 (toluene:acetone = 5:1); \textbf{melting point} = 53-54 °C; \textit{\(^{1}H\) NMR} (400 MHz, CDCl\(_3\)) \(\delta\) ppm: 3.36 (s, 3H, H-1), 3.54-3.56 (m, 2H, H-2), 3.80-3.82 (m, 2H, H-3), 5.26 (s, 2H, H-4), 7.24 (\textit{dd}, 1.2, 4.9 and 8.0 Hz, 2H, H-16/23), 7.28 (\textit{d}, 1.2 Hz, 2H, H-6/10), 7.45 (\textit{t}, 1.6 Hz, 1H, H-8), 7.51 (\textit{dt}, 1.2 and 7.8 Hz, 2H, H-15/22) and 8.60 (\textit{dd}, 0.9, 1.8 and 4.9 Hz, 2H, H-17/24); \textit{\(^{13}C\) NMR} (100 MHz, CDCl\(_3\)) \(\delta\) ppm: 59.1 (C-1), 68.0 (C-3), 71.6 (C-2), 88.0 (C-12/19), 89.1 (C-11/18), 93.6 (C-4), 120.6 (C-6/10), 123.1 (C-16/23), 123.8 (C-7/9), 127.4 (C-14/21), 129.2 (C-8), 136.3 (C-15/22), 143.1 (C-13/20), 150.2 (C-17/24) and 157.0 (C-5); \textbf{FTIR} (neat) \(\nu_{\text{max}}\) (cm\(^{-1}\)): 3054 (w, Ar C–H stretch), 2213 (w, C\(\equiv\)C stretch) and [1579, 1559, 1478, 1457, 1429 (m, Ar C=C and C=N stretch)]; \textbf{UV/Vis} (CH\(_2\)Cl\(_2\)) \(\lambda_{\text{max}}\) (nm): 271, 297 and 304 (log \(\varepsilon\) 4.60, 4.73 and 4.73); \textbf{Fluorescence} (CH\(_2\)Cl\(_2\), \(\lambda_{\text{exc}}\) 376 nm) \(\lambda_{\text{ems}}\) (nm): 354, \textbf{ESI-MS} [M+H]\(^+\) \(m/z = 385\); \textbf{HRMS} Calcd for C\(_{24}\)H\(_{21}\)N\(_2\)O\(_3\) [M+H]\(^+\): 385.1547, Found: 385.1547.
Experimental

3,5-bis(Pyridin-2-ylethynyl)phenol (131)

Compound 109 (0.1421 g, 1 mmol, 1.0 equiv.), 2-bromopyridine (0.23 mL, 2.4 mmol, 2.4 equiv.), piperidine (0.39 mL, 4 mmol, 4.0 equiv.), PdCl₂ (0.0180 g, 0.1 mmol, 10 mol%), PPh₃ (0.1301 g, 0.5 mmol, 20 mol%) and acetone/water (3:3 g) were treated as described in General Procedure C. Purification by flash column chromatography (SiO₂, hexane/aceton = 4:1 and then CH₂Cl₂/MeOH = 80:1) afforded 131 (0.1503 g, 52%) as a pale yellow powder.

\[
\text{TLC } R_f = 0.20 \text{ (hexane/aceton = 4:1) and 0.18 (CH}_2\text{Cl}_2/\text{MeOH = 40:1); melting point} = 181-182 \degree \text{C; } ^1\text{H NMR} \text{ (400 MHz, CDCl}_3) \delta \text{ ppm: 7.25 (t, 1.2 Hz, 1H, H-4), 7.27 (d, 1.2 Hz, 2H, H-2/6), 7.30 (ddd, 1.2, 5.0 and 7.4 Hz, 2H, H-12/21), 7.54 (dt, 1.2 and 7.8 Hz, 2H, H-10/19), 7.73 (dd, 1.8 and 7.8 Hz, 2H, H-11/20), 8.59 (ddd, 0.9, 1.8 and 5.0 Hz, 2H, H-13/22) and 10.54 (br s, 1H, OH); } ^13\text{C NMR} \text{ (100 MHz, CDCl}_3) \delta \text{ ppm: 87.7 (C-8/15), 90.0 (C-7/14), 120.7 (C-2/6), 123.2 (C-12/21), 123.3 (C-3/5), 127.0 (C-4), 127.9 (C-10/19), 137.2 (C-11/20), 142.8 (C-9/16), 149.4 (C-13/22) and 157.5 (C-1); FTIR (neat) } \nu_{\text{max}} \text{ (cm}^{-1}) \text{: 3050 (w, Ar C–H stretch), 2213 (m, C} \equiv \text{C stretch), [1581, 1557, 1490, 1467 (m, Ar C=C and C=N stretch), 1366 (m, sp}^3 \text{ C–H bend) and 1142 (m, C–O stretch); UV/Vis (CH}_2\text{Cl}_2) \lambda_{\text{max}} \text{ (nm): 272, 296 and 320 (log } \varepsilon \text{ 4.63, 4.78 and 4.17); Fluorescence (CH}_2\text{Cl}_2, \lambda_{\text{exc}} \text{ 333 nm) } \lambda_{\text{ems}} \text{ (nm): 356; ESI-MS [M+H] }^+ \text{ m/z = 298; HRMS Calcd for } C_{20}H_{13}N_2O [M+H] }^+ \text{: 297.1022, Found: 297.1023.}
\]

1,3-bis((4-Fluorophenyl)ethynyl)benzene (132)

4-Fluoriodobenzene (1.02 mL, 8.8 mmol, 1.0 equiv.), 1,3-diethynylbenzene (0.53 mL, 4.0 mmol, 0.45 equiv.), Pd(PPh₃)₂Cl₂ (0.3089 g, 0.44 mmol, 5 mol%), CuI (0.1676 g, 0.88 mmol, 10%), Et₃N (30 mL) and anhydrous toluene (15 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO₂, hexane) afforded 132 (1.0176 g, 81%) as a white powder.

\[
\text{TLC } R_f = 0.29 \text{ (hexane); melting point} = 153-154 \degree \text{C (lit.}^{165} 140-142 \degree \text{C); } ^1\text{H NMR} \text{ (400 MHz, CDCl}_3) \delta \text{ ppm: 7.04-7.08 (m, 4H, H-11/13/19/21), 7.34 (t, 7.7 Hz, 1H, H-5), 7.48-7.54 (m, 6H, H-4/6/10/14/18/22) }
\]
and 7.70 (s, 1H, H-2); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 88.3 (C-7/15), 89.1 (C-8/16), 115.8 ($d$, $^2$J$_{C-F}$ = 8.3 Hz, C-11/13/19/21), 119.2 ($d$, $^4$J$_{C-F}$ = 3.6 Hz, C-9/17), 123.6 (C-1/3), 128.7 (C-5), 131.4 (C-4/6), 134.1 ($d$, $^3$J$_{C-F}$ = 7.6 Hz, C-1/14/18/22), 134.6 (C-2) and 162.7 ($d$, $^1$J$_{C-F}$ = 248.2 Hz, C-12/20); $^{19}$F NMR (470 MHz, CDCl$_3$) δ ppm: -110.54; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3063 (w, Ar C–H stretch), [1567, 1504 (m, Ar C=C stretch)] and 1217 (m, Ar C–F stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 283 and 298 (log $\varepsilon$ 4.81 and 4.74); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 370 nm) $\lambda_{\text{em}}$ (nm): 414, 437 and 464; APCI-MS [M+CH$_3$OH+H]$^+$ m/z = 347; HRMS Calcd for C$_{22}$H$_{12}$F$_2$ [M]$^+$: 314.0902, Found: 314.0900.

Data collected matched the reported data, full NMR assignment made by the author.

3,5-bis((4-Fluorophenyl)ethynyl)phenol (133)

4-Fluoroiodobenzene (0.25 mL, 2.12 mmol, 1.0 equiv.), 109 (0.1371 g, 0.97 mmol, 0.45 equiv.), Pd(PPh$_3$)$_2$Cl$_2$ (0.0750 g, 0.11 mmol, 10 mol%), CuI (0.0410 g, 0.21 mmol, 20 mol%), Et$_3$N (7.5 mL) and anhydrous toluene (2.5 mL) were treated as described in General Procedure A. THF (1 mL) was also added in the reaction to improve the solubility of the phenol. Purification by flash column chromatography (SiO$_2$, hexane/CH$_2$Cl$_2$ = 1:1) afforded 133 (0.2298 g, 72%) as a yellow to brown solid.

TLC $R_f$ = 0.30 (hexane/CH$_2$Cl$_2$ = 1:2); melting point = 157-158 °C; $^1$H NMR (400 MHz, acetone-$d_6$) δ ppm: 7.04 ($d$, 1.6 Hz, 2H, H-2/6), 7.18-7.24 (m, 5H, H-4/11/13/19/21), 7.60-7.65 (m, 4H, H-10/14/18/22) and 8.93 (s, 1H, 1-OH); $^{13}$C NMR (100 MHz, acetone-$d_6$) δ ppm: 88.8 ($d$, $^5$J$_{C-F}$ = 1.6 Hz, C-8/16), 89.2 (C-7/15), 116.6 ($d$, $^2$J$_{C-F}$ = 22.1 Hz, C-11/13/19/21), 119.3 (C-2/6) 120.0 ($d$, $^4$J$_{C-F}$ = 3.5 Hz), 125.4 (C-3/5), 126.7 (C-4), 134.6 ($d$, $^3$J$_{C-F}$ = 8.3 Hz), 158.3 (C-1) and 163.5 ($d$, $^1$J$_{C-F}$ = 246.7 Hz, C-12/20); $^{19}$F NMR (376 MHz, acetone-$d_6$) δ ppm: -111.95; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3304 (m, brd, O–H stretch), 3059 (w, Ar C–H stretch), [1596, 1579, 1508 (s, Ar C=C stretch)], 1211 (s, Ar C–F stretch) and 1156 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 283, 296 and 320 (log $\varepsilon$ 4.85, 4.71 and 4.02); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 319 nm) $\lambda_{\text{em}}$ (nm): 352; ESI-MS [2M-H]$^-$ m/z = 659; HRMS Calcd for C$_{22}$H$_{13}$F$_2$O [M+H]$^+$: 331.0934, Found: 331.0924.
Experimental

1,3-bis((2-Fluorophenyl)ethynyl)benzene (134)

2-Fluoroiodobenzene (1.03 mL, 8.8 mmol, 1.0 equiv.), 1,3-diethynylbenzene (0.53 mL, 4.0 mmol, 0.45 equiv.), Pd(PPh₃)₂Cl₂ (0.3089 g, 0.44 mmol, 10 mol%), CuI (0.1676 g, 0.88 mmol, 20 mol%), Et₃N (40 mL) and anhydrous toluene (20 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO₂, hexane) afforded 134 (0.7574 g, 60%) as a white solid.

**TLC R_f = 0.25 (hexane); melting point = 100-101 °C;**

**¹H NMR (400 MHz, CDCl₃) δ ppm:** 7.10-7.16 (m, 4H, H-11/13/19/21), 7.31-7.38 (m, 3H, H-5/12/20), 7.51-7.55 (m, 4H, H-4/6/10/18) and 7.78 (t, 1.6 Hz, 1H, H-2);

**¹³C NMR (100 MHz, CDCl₃) δ ppm:** 83.5 (C-8/16), 93.6 (d, J_C-F = 2.8 Hz, C-7/15), 111.7 (d, J_C-F = 20.3 Hz, C-9/17), 115.7 (d, J_C-F = 20.3 Hz, C-13/21), 123.4 (C-1/3), 124.1 (d, J_C-F = 3.6 Hz, C-11/19), 128.6 (C-5), 130.3 (d, J_C-F = 7.6 Hz, C-12/20), 131.8 (C-4/6), 133.6 (C-10/18), 134.8 (C-2) and 162.8 (d, J_C-F = 250.4 Hz, C-14/22);

**¹⁹F NMR (470 MHz, CDCl₃) δ ppm:** -109.64;

**FTIR (neat) ν_{max} (cm⁻¹):** [3077, 3061, 3032 (w, Ar C–H stretch)], [1591, 1571, 1493 (m, Ar C=C stretch)] and 1215 (m, Ar C–F stretch);

**UV/Vis (CH₂Cl₂) $\lambda_{max}$ (nm):** 283, 302 and 323 (log ε 4.86 and 4.76);

**Fluorescence (CH₂Cl₂, $\lambda_{exc}$ 319 nm) $\lambda_{ems}$ (nm):** 335 and 345;

**APCI-MS [M+CH₃OH+H]^+ m/z** = 347;


3,5-bis((2-Fluorophenyl)ethynyl)phenol (135)

2-Fluoroiodobenzene (0.26 mL, 2.2 mmol, 1.0 equiv.), 109 (0.1422 g, 1.0 mmol, 0.45 equiv.), Pd(PPh₃)₂Cl₂ (0.0770 g, 0.11 mmol, 10 mol%), CuI (0.0420 g, 0.22 mmol, 20 mol%), Et₃N (7.5 mL) and anhydrous toluene (2.5 mL) were treated as described in General Procedure A. THF (2 mL) was also added in the reaction to improve the solubility of the phenol. Purification by flash column chromatography (SiO₂, hexane/CH₂Cl₂ = 1:1) afforded 135 (0.1959 g, 59%) as a yellow solid.

**TLC R_f = 0.33 (hexane/CH₂Cl₂ = 1:1); melting point = 142-143 °C;**

**¹H NMR (400 MHz, acetone-d₆) δ ppm:**

7.09 (d, 1.6 Hz, 2H, H-2/6), 7.24-7.29 (m, 5H, H-4/11/13/19/21), 7.46-7.51 (m, 2H, H-12/20) and 7.61-
Experimental

7.66 (m, 2H, H-10/18) and 9.01 (s, 1H, 1-OH); $^{13}$C NMR (100 MHz, acetone-$d_6$) δ ppm: 83.6 (C-8/16), 94.0 ($^4$J$_{C-F}$ = 2.8 Hz, C-7/15), 112.0 ($^2$J$_{C-F}$ = 15.5 Hz, C-9/17), 116.4 ($^2$J$_{C-F}$ = 20.4 Hz, C-13/21), 119.6 (C-2/6), 125.2 (C-3/5), 125.4 ($^4$J$_{C-F}$ = 3.7 Hz, C-11/19), 126.7 (C-4), 131.8 ($^3$J$_{C-F}$ = 7.7 Hz, C-12/20), 134.5 (C-10/18), 158.4 (C-1) and 163.4 ($^1$J$_{C-F}$ = 248.5 Hz, C-14/22); $^{19}$F NMR (376 MHz, acetone-$d_6$) δ ppm: -111.45; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3284 (m, brd, O–H stretch), 3060 (w, Ar C–H stretch), [1573, 1492 (m, Ar C=C stretch)], 1203 (m, Ar C–F stretch) and 1154 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 281, 300 and 323 (log $\varepsilon$ 4.75, 4.69 and 4.05); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 339 nm) $\lambda_{\text{ems}}$ (nm): 354; ESI-MS [2M-H]$^+$ $m/z$ = 659; HRMS Calcd for C$_{22}$H$_{13}$F$_2$O [M+H]$^+$: 331.0934, Found: 331.0935.

6.4 Synthesis of Substituted Tetraarylcyclopentadienone Derivatives

3,4-bis(4-Bromophenyl)-2,5-diphenylcyclopenta-2,4-dienone (142)

4,4'-Dibromobenzil (3.68 g, 10.0 mmol, 1.0 equiv.), 1,3-diphenyl-2-propanone (2.10 g, 10.0 mmol, 1.0 equiv.) and EtOH (20 mL) as well as KOH (0.29 g, 5.2 mmol) and EtOH (5 mL) were treated as described in General Procedure D. The resulting precipitate of 142 (4.49 g, 83%) obtained after precipitation at 0 °C was collected by filtration under vacuum as a dark purple powder.

TLC $R_f$ = 0.45 (hexane/EtOAc = 15:1); melting point = 248-249 °C (lit.$^{166}$ 249.0-249.5 °C); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 6.82 ($^d$ 8.8 Hz, 4H, H-12/14/19/21), 7.21-7.23 (m, 4H, H-5/7/26/28), 7.27-7.29 (m, 6H, H-4/6/8/25/27/29) and 7.37 ($^d$ 8.8 Hz, 4H, H-11/15/18/22);

$^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 123.2 (C-13/20), 125.9 (C-2/23), 127.9 (C-6/27), 128.3 (C-4/8/25/29), 130.1 (C-5/7/26/28), 130.2 (C-3/24), 131.0 (C-12/14/19/21), 131.5 (C-11/15/18/22), 131.7 (C-10/17), 152.6 (C-9/16) and 199.6 (C-1); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3048 (w, Ar C–H stretch), 1709 (s, C=O stretch), [1595, 1583, 1567, 1480 (m, Ar C=C stretch)] and 1072 (m, Ar C–Br stretch); ESI-MS [M+Na]$^+$ $m/z$ = 563 (51%), 564 (14%), 565 (100%), 566 (31%), 567 (48%), 568 (14%) and 569 (1%); HRMS Calcd for C$_{29}$H$_{18}$O$_7$Br$_2$Na [M+Na]$^+$ (monoisotopic): 562.9617, Found: 562.9618.

Data collected matched the reported data.$^{86,166}$ full NMR assignment made by the author.
3,4-bis(4-Fluorophenyl)-2,5-diphenylcyclopenta-2,4-dienone (143)

4,4'-Difluorobenzil (5.00 g, 20.3 mmol, 1.0 equiv.), 1,3-diphenyl-2-propanone (4.27 g, 20.3 mmol, 1.0 equiv.) and EtOH (30 mL) as well as KOH (0.57 g, 10.2 mmol) and EtOH (20 mL) were treated as described in General Procedure D. Purification was performed after the solvent had been removed under vacuum by flash column chromatography (SiO$_2$, hexane/EtOAc = 15:1) afforded 143 (7.10 g, 83%) as a dark purple powder.

TLC $R_f$ = 0.38 (hexane/EtOAc = 15:1); melting point = 235-236 °C (lit.$^{44}$ 235.8-235.9 °C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 7.21-7.30 ($m$, 10H, H-4/5/6/7/8/25/26/27/28/29) and 6.91 ($d$, 7.2 Hz, 8H, H-11/12/14/15/18/19/21/22); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 115.5 ($d$, $^2J_{C-F}$ = 21.6 Hz, C-12/14/19/21), 125.7 (C-2/23), 127.8 (C-6/27), 128.3 (C-4/8/25/29), 129.0 ($d$, $^3J_{C-F}$ = 3.4 Hz, C-11/15/18/22), 130.2 (C-5/7/26/28), 130.6 (C-3/24), 131.5 ($d$, $^4J_{C-F}$ = 8.1 Hz, C-10/17), 153.1 (C-9/16), 162.8 ($d$, $^1J_{C-F}$ = 248.5 Hz, C-13/20) and 200.0 (C-1); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -111.56; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3046 (w, Ar C–H stretch), 1715 (m, Ar C=O stretch), [1599, 1569, 1502, 1491 (m, Ar C=C stretch)] and 1223 (m, Ar C–F stretch); APCI-MS [M+H]$^+$ m/z = 421 (100%); HRMS Calcd for C$_{29}$H$_{19}$F$_2$O [M+H]$^+$: 421.1404, Found: 421.1423.

Data collected matched the reported data,$^{44}$ full NMR assignment made by the author.

6.5 Synthesis of Pentaaryl Dendrimers

6.5.1 Synthesis of Symmetrical Pentaaryl Dendrimers

*Dendrimer Penta-H-Br-Br (150)*

1,3-Diethynylbenzene (0.067 mL, 0.5 mmol, 1.0 equiv.), 142 (0.8130 g, 1.5 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 24 h. The resulting reaction mixture was then added dropwise into ethanol (100 mL) and cooled to 0 °C using an ice bath for an hour. The precipitate formed was collected by filtration under vacuum and washed with cold ethanol. The crude product was then recrystallised from hexane to obtain 150 (0.3460 g, 60%) as a pale yellow powder.
Experimental

Melting point = > 300 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 6.61 (d, 8.4 Hz, 4H, H-22/24/55/57), 6.70 (d, 8.4 Hz, 4H, H-15/17/48/50), 6.72-6.75 (m, 4H, H-29/31/62/64), 6.86-6.94 (m, 9H, H-2/28/32/34/36/61/62/65), 7.03 (t, 8.4 Hz, 4H, H-21/25/54/58), 7.08-7.12 (m, 9H, H-1/8/10/14/18/41/43/47/51), 7.19-7.23 (m, 6H, H-7/9/11/40/42/44) and 7.26 (s, 2H, H-33/66); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 120.0 (C-23/56), 120.2 (C-16/49), 126.1 (C-30/63), 126.7 (C-9/42), 127.0 (C-34), 127.3 (C-28/32/61/65), 127.9 (C-7/11/40/44), 128.1 (C-2/36), 130.0 (C-8/10/41/43), 130.2 (C-21/25/54/58), 130.5 (C-14/18/47/51), 131.5 (C-29/31/62/64), 131.7 (C-1), 133.1 (C-15/17/48/50), 131.9 (C-33/66), 133.1 (C-22/24/55/57), [(137.8, 138.7, 139.1, 139.3, 139.5, 140.2, 140.9, 141.0, 141.2), quarternary Ar-C]; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3058, 3027 (w, Ar C–H stretch)], [1599, 1574, 1488 (w, Ar C=C stretch)] and 1071 (m, Ar C–B r stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$(nm): 253 and 280 (log $\varepsilon$ 5.06 and 4.70); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$(nm): 412, 436 and 463; MALDI-TOF-MS (dithranol) Calcd for C$_{66}$H$_{32}$Br$_4$Na [M+Na]$^+$: 1177 (100%), Found: 1177 (100%).

Dendrimer Penta-H-F-F (151)

1,3-Diethynylbenzene (0.026 mL, 0.2 mmol, 1.0 equiv.), 143 (0.2520 g, 0.6 mmol, 3.0 equiv.) and anhydrous o-xylene (1 mL) were treated as described in General Procedure E at 200 °C overnight. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 100:0 to 98:2) afforded 151 (0.1109 g, 61%) as a pale yellow powder. TLC $R_f$ = 0.20 (hexane/EtOAc = 97.5:2.5); melting point = > 300 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 6.55-6.60 (m, 4H, H-22/24/55/57), 6.62-6.69 (m, 8H, H-15/17/21/25/48/50/54/58), 6.71-6.78 (m, 8H, H-14/18/29/31/47/51/62/64), 6.83-6.92 (m, 9H, H-2/28/30/32/34/36/61/63/66), 7.08-7.11 (m, 5H, H-1/8/10/41/43), 7.15-7.22 (m, 6H, H-7/9/11/40/42/44) and 7.25 (s, 2H, H-33/66); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 113.9 (d, 2J$_{C,F}$ = 21.2 Hz, C-22/24/55/57), 114.2 (d, 2J$_{C,F}$ = 21.2 Hz, C-15/17/48/50), 126.0 (C-30/63), 126.6 (C-9/42), 126.6 (C-34), 127.3 (C-28/32/61/65), 127.8 (C-7/11/40/44), 128.1 (C-2/36),
Experimental

130.1 (C-8/10/41/43), 131.6 (C-29/31/62/64), 131.7 (C-33/66), 131.8 (C-1), 132.9 (d, $^3J_{C-F} = 8.1$ Hz, C-21/25/54/58), 133.0 (d, $^3J_{C-F} = 8.1$ Hz, C-14/18/47/51), 135.9 (d, $^4J_{C-F} = 3.3$ Hz, C-13/46), 136.2 (d, $^4J_{C-F} = 3.3$ Hz, C-20/53), [(138.3, 139.5, 139.8, 140.7, 140.9, 141.0, 141.1, 141.5), quarternary Ar-C], 160.9 (d, $^1J_{C-F} = 243.8$ Hz, C-23/56) and 161.1 (d, $^1J_{C-F} = 243.8$ Hz, C-16/49); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -116.85 and -116.56; FTIR (neat) $\nu_{\text{max}}$ $(\text{cm}^{-1})$: [3054, 3024 (w, Ar C–H stretch)], [1602, 1511 (m, Ar C=C stretch)] and 1220 (m, Ar C–F stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ $(\text{nm})$: 251 and 278 (log $\varepsilon$ 4.95 and 4.62); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 356 nm) $\lambda_{\text{ems}}$ $(\text{nm})$: 412, 436 and 463; MALDI-TOF-MS (dithranol) Calcd for C$_{66}$H$_{42}$F$_4$Na [M+Na]$^+$: 933 (100%), Found: 933 (100%).

Dendrimer Penta-OMEM-Br-Br (152)

Compounds 108 (0.0575 g, 0.25 mmol, 1.0 equiv.), 142 (0.4065 g, 0.75 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 24 h. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 4:1 to 0:1) afforded 152 (0.2410 g, 77%) as a yellow powder. TLC $R_f$ = 0.30 (hexane/EtOAc = 4:1); melting point = 147-148 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 3.32 (s, 3H, H-70), 3.43-3.46 (m, 2H, H-69), 3.56-3.58 (m, 2H, H-68), 4.78 (s, 2H, H-67), 6.52 (d, 1.6 Hz, 2H, H-2/36), 6.58 (d, 8.8 Hz, 4H, H-22/24/55/57), 6.67 (d, 8.8 Hz, 4H, H-15/17/48/50), 6.69-6.72 (m, 8H, H-8/10/14/18/41/43/47/51), 7.01 (d, 8.8 Hz, 4H, H-21/25/54/58), 7.06-7.09 (m, 8H, H-28/30/32/61/63/65), 7.16-7.22 (m, 6H, 7/9/11/40/42/44) and 7.22 (s, 2H, H-33/66); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 59.1 (C-70), 67.7 (C-68), 71.7 (C-69), 93.6 (C-67), 116.3 (C-2/36), 119.9 (C-23/56), 120.3 (C-16/49), 125.6 (C-34), 126.1 (C-30/63), 126.7 (C-9/42), 127.4 (C-28/32/61/65), 127.9 (C-7/11/40/44), 130.0 (C-8/10/41/43), 130.2 (C-21/25/54/58), 130.5 (C-14/18/47/51), 131.5 (C-29/31/62/64), 131.8 (C-33/66), 133.0 (C-22/24/55/57), 133.1 (C-15/17/48/50), [(137.9, 138.7, 139.1, 139.3, 139.6, 140.2, 140.8, 140.9, 141.2, 142.1), quarternary Ar-C] and 155.9 (C-1); FTIR (neat) $\nu_{\text{max}}$ $(\text{cm}^{-1})$: [3053, 3025 (w, Ar C–H stretch)], [2961, 2922, 2874 (w, sp$^3$ C–H stretch)], [1586, 1487 (m, Ar C=C stretch)], 1388 (w, sp$^3$ C–H bend), 1188 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$
Experimental

(nm): 254 and 281 (log ε 5.02 and 4.70); **Fluorescence** (CH$_2$Cl$_2$, $\lambda_{exc}$ 376 nm) $\lambda_{ems}$ (nm): 413, 438 and 464; **MALDI-TOF-MS** (dithranol) Calcd for C$_{70}$H$_{50}$Br$_4$O$_3$Na [M+Na]$^+$: 1281 (100%), Found: 1281 (100%).

**Dendrimer Penta-OH-Br-Br (153)**

**Through Deprotection Reaction of Penta-OMEM-Br-Br (152)**

Compound 152 (0.0127 g, 0.01 mmol) and CH$_2$Cl$_2$ (1 mL) were added into a 5 mL round bottom flask and stirred. Anhydrous ZnBr$_2$ (0.0225 g, 0.1 mmol, 10 equiv.) was then added into the solution and the reaction mixture was stirred at room temperature. The reaction was judged to be complete after no more starting material was observed by TLC. The resulting mixture was then washed with saturated NaHCO$_3$ and brine, dried (MgSO$_4$) and concentrated to give dendrimer 153 (0.0099 g, 85%) as a yellow powder.

**Through Diels-Alder Cycloaddition Reaction**

Compounds 109 (0.0500 g, 0.35 mmol, 1.0 equiv.), 142 (0.5690 g, 1.05 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 3 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 6:1) afforded 153 (0.3226 g, 78%) as a yellow powder.

**Data for both methods:**

<table>
<thead>
<tr>
<th>Compound</th>
<th>TLC R$_f$</th>
<th>Melting point</th>
<th>$^1$H NMR (400 MHz, CDCl$_3$) δ ppm</th>
<th>$^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm</th>
</tr>
</thead>
</table>
| 153      | 0.28     | 226-227 °C    | 4.43 (br s, 1H, OH), 6.33 (d, 8.6 Hz, 2H, H-2/36), 6.58 (d, 8.6 Hz, 4H, H-22/24/55/57), 6.61 (t, 1.6 Hz, 1H, H-34), 6.67 (d, 9.2 Hz, 4H, H-15/17/48/50), 6.70-6.72 (m, 4H, H-29/31/62/64), 6.86-6.94 (m, 6H, H-28/30/32/61/63/65), 7.01 (d, 8.6 Hz, 4H, H-21/25/54/58), 7.06-7.07 (m, 4H, H-14/18/47/51), 7.08-7.09 (m, 4H, H-8/10/41/43), 7.19-7.21 (m, 6H, H-7/9/11/40/42/44) and 7.22 (s, 2H, H-33/66); | 115.2 (C-2/36), 119.9 (C-23/56), 120.3 (C-16/49), 124.8 (C-34), 126.2 (C-30/63), 126.7 (C-9/42), 127.4 (C-28/32/61/65), 127.9 (C-7/11/40/44), 130.0 (C-8/10/41/43), 130.2 (C-21/25/54/58), 130.5 (C-14/18/47/51), 131.4 (C-29/31/62/64), 131.8 (C-33/66), 133.0 (C-22/24/55/57), 133.1 (C-15/17/48/50), [137.9, 138.7, 139.1, 139.2, 139.4, 140.2, 140.6, 141.0, 141.1, 142.4), quarternary Ar-C] and 154.2; **FTIR** (neat) $\nu_{max}$ (cm$^{-1}$): 3562 (w, O–H stretch), [3055, 3025 (w, Ar C–H stretch)], [1592, 239] }
Experimental

1574, 1487 (m, Ar C=C stretch), 1173 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH₂Cl₂) λmax (nm): 253 and 281 (log ε 5.11 and 4.77); Fluorescence (CH₂Cl₂, λexc 376 nm) λems (nm): 414, 438 and 464; MALDI-TOF-MS (dithranol) Calcd for C₆₆H₄₂Br₄ONa [M+Na]⁺: 1193.0 (100%), Found: 1193.4 (100%).

Dendrimer Penta-OH-F-F (154)

Compounds 109 (0.1704 g, 1.2 mmol, 1.0 equiv.), 143 (1.5120 g, 3.6 mmol, 3.0 equiv.) and anhydrous o-xylene (3 mL) were treated as described in General Procedure E at 200 °C overnight. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 95:5 to 80:20) afforded 154 (1.0220 g, 92%) as a yellow powder.

TLC Rf = 0.06 (hexane/EtOAc = 9:1); melting point = 175-176 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: 4.62 (s, 1H, OH), 6.35 (d, 1.2 Hz, 2H, H-2/36), 6.55-6.60 (m, 4H, H-22/24/55/57), 6.62-6.69 (m, 9H, H-15/17/21/25/34/48/50/54/58), 6.73-6.78 (m, 8H, H-14/18/29/31/47/51/62/64), 6.85-6.93 (m, 6H, H-28/30/32/61/63/65), 7.09-7.11 (m, 4H, H-8/10/41/43), 7.16-7.22 (m, 6H, H-7/9/11/40/42/44) and 7.24 (s, 2H, H-33/66); ¹³C NMR (100 MHz, CDCl₃) δ ppm: 113.9 (d, ²JCF = 21.2 Hz, C-22/24/55/57), 114.3 (d, ²JCF = 21.2 Hz, C-15/17/48/50), 115.2 (C-2/36), 124.9 (C-34), 126.1 (C-30/63), 126.6 (C-9/42), 127.3 (C-28/32/61/65), 127.8 (C-7/11/40/44), 130.1 (C-8/10/41/43), 131.5 (C-29/31/62/64), 131.6 (C-33/66), 132.9 (d, ³JCF = 8.2 Hz, C-21/25/54/58), 133.0 (d, ³JCF = 8.2 Hz, C-14/18/47/51), 135.8 (d, ⁴JCF = 3.6 Hz, H-13/46), 136.2 (d, ⁴JCF = 3.6 Hz, C-20/53), [(138.5, 139.4, 139.7, 140.4, 140.7, 141.0, 141.4, 142.6), quaternary Ar-C], 154.2 (C-1), 160.9 (d, ¹JCF = 243.8 Hz, C-23/56) and 161.1 (d, ¹JCF = 243.8 Hz, C-16/49); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm: -116.77 and -116.48; FTIR (neat) νmax (cm⁻¹): 3543 (w, O–H stretch), [3049, 3025 (w, Ar C–H stretch), [1593, 1510 (m, Ar C=C stretch)], 1221 (m, Ar C–F stretch) and 1178 (w, C–O stretch); UV/Vis (CH₂Cl₂) λmax (nm): 251 and 278 (log ε 5.07 and 4.70); Fluorescence (CH₂Cl₂, λexc 376 nm) λems (nm): 413, 437 and 464; MALDI-TOF-MS (dithranol) Calcd for C₆₈H₄₂F₄O [M⁺]: 926.3 (100%), Found: 926.3 (100%).
6.5.2 Synthesis of Pentaaryl Dendrimer Monoadducts

**Monoadduct MonoPenta-H-Br-Acetylene (155)**

Compound **142** (0.3613 g, 0.67 mmol, 1.0 equiv.), 1,3-diethynylbenzene (0.14 mL, 1.0 mmol, 1.5 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 2 h. Purification by flash column chromatography (SiO₂, hexane/Et₂O = 99:1) afforded **155** (0.2983 g, 70%) as a pale yellow powder.

**TLC** R_f = 0.36 (hexane/Et₂O = 96:4); **melting point** = 219-220 °C; **¹H NMR** (400 MHz, CDCl₃) δ ppm: 3.00 (s, 1H, H-38), 6.68 (d, 8.6 Hz, 2H, H-22/24), 6.74 (d, 8.6 Hz, 2H, H-15/17), 6.83-6.87 (m, 2H, H-29/31), 6.99-7.02 (m, 3H, H-28/30/32), 7.04 (t, 1.6 Hz, 1H, H-1), 7.06-7.09 (m, 3H, H-2/21/25), 7.11-7.16 (m, 4H, H-8/10/14/18), 7.20-7.23 (m, 3H, H-7/9/11), 7.30 (dt, 1.6 and 7.2 Hz, 1H, H-36), 7.42 (t, 1.6 Hz, 1H, H-34) and 7.57 (s, 1H, H-33); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 77.2 (C-38), 83.6 (C-37), 120.1 (C-23), 120.4 (C-16), 121.8 (C-35), 126.3 (C-2), 126.3 (C-30), 126.8 (C-9), 127.5 (C-28/32), 127.7 (C-1), 128.0 (C-7/11), 129.9 (C-8/10), 130.3 (C-21/25), 130.3 (C-36), 130.5 (C-14/18), 131.4 (C-29/31), 131.8 (C-33), 133.0 (C-22/24), 133.1 (C-15/17), 133.5 (C-34), [(138.2, 138.7, 139.0, 139.2, 139.5, 140.3, 140.4, 141.1, 141.1, 141.6), quarternary Ar-C]; **FTIR** (neat) ν_max (cm⁻¹): 3296 (w, sp ≡C–H stretch), [3053, 3025 (w, Ar C–H stretch)], 1597, 1488 (m, Ar C=C stretch) and 1071 (m, Ar C–Br stretch); **UV/Vis** (CH₂Cl₂) λ_max (nm): 249 and 281 (log ε 5.02 and 4.51); **Fluorescence** (CH₂Cl₂, λ_exc 376 nm) λ_ems (nm): 413, 438 and 464; **HRMS** Calcd for C₃₈H₂₄⁷⁹Br₂ [M+H]^⁺ (monoisotopic): 638.0239, Found: 638.0242.

**Monoadduct MonoPenta-OH-Br-Acetylene (156)**

Compounds **143** (0.4472 g, 0.83 mmol, 1.0 equiv.), **109** (0.1065 g, 0.75 mmol, 1.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 2 h. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 97.5:2.5 to 95:5) afforded **156** (0.2737 g, 56%) and dimer by-product **153** (0.2544 g, 29%) both as yellow powders.
**Experimental**

**TLC R**<sub>f</sub> = 0.11 (hexane/EtOAc = 9:1); **melting point** = 240-241 °C; **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ ppm: 2.97 (s, 1H, H-38), 4.86 (s, 1H, OH), 6.49 (dd, 1.6 and 2.4 Hz, 1H, H-2), 6.63 (d, 8.6 Hz, 2H, H-22/24), 6.70 (d, 8.6 Hz, 2H, H-15/17), 6.75 (dd, 1.6 and 2.4 Hz, 1H, H-36), 6.81-6.83 (m, 2H H-29/31), 6.96 (t, 1.6 Hz, 1H, H-34), 6.98-7.02 (m, 3H, H-28/30/32), 7.04 (d, 8.6 Hz, 2H, H-21/25), 7.08-7.12 (m, 4H, H-8/10/14/18), 7.18-7.21 (m, 3H, H-7/9/11) and 7.52 (s, 1H, H-33); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ ppm: 77.4 (C-38), 83.2 (C-37), 117.2 (C-36), 118.1 (C-2), 120.1 (C-23), 120.4 (C-16), 122.8 (C-8/10), 131.3 (C-29/31), 130.3 (C-21/25), 130.6 (C-14/18), 131.7 (C-33), 133.0 (C-22/24), 133.1 (C-15/17), [138.4, 138.6, 139.0, 139.4, 139.1, 139.9, 140.5, 141.1, 141.1, 143.3, quarternary Ar-C] and 154.7 (C-1); **FTIR** (neat) υ<sub>max</sub> (cm<sup>-1</sup>): 3559 (m, O–H stretch), 3284 (m, sp≡C–H stretch), [3055, 3024 (w, Ar C–H stretch), [1589, 1487 (m, Ar C=C)], 1183 (m, C–O stretch) and 1070 (m, Ar C–Br stretch); **UV/Vis** (CH<sub>2</sub>Cl<sub>2</sub>) λ<sub>max</sub> (nm): 249, 281 and 303 (log ε 4.98, 4.48 and 4.06); **Fluorescence** (CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>exc</sub> 376 nm) λ<sub>ems</sub> (nm): 413, 438 and 465; **HRMS** Calcd for C<sub>38</sub>H<sub>24</sub>Br<sub>2</sub>O [M]<sup>+</sup> (monoisotopic): 654.0188, Found: 654.0174.

### 6.5.3 Synthesis of Unsymmetrical Pentaaryl Dendrimer

**Dendrimer Penta-H-Br-F (157)**

Monoadduct 155 (0.0983 g, 0.15 mmol, 1.0 equiv.), 143 (0.0650 g, 0.15 mmol, 1.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E 200 °C overnight. Purification by flash column chromatography (SiO<sub>2</sub>, hexane/EtOAc = 99:1) afforded 157 (0.1211 g, 76%) as a yellow powder.

**TLC R**<sub>f</sub> = 0.15 (hexane/EtOAc = 97.5:2.5); **melting point** = 241-242 °C; **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ ppm: 6.57-6.80 (m, 16H, H-15/17/22/24/29/31/47/48/50/51/54/55/57/58/62/64), 6.85-6.94 (m, 9H, H-2/28/30/32/34/36/61/63/65), 7.03 (d, 8.5 Hz, 2H, H-21/25), 7.09-7.13 (m, 7H, H-1/8/10/14/18/41/43), 7.18-7.22 (m, 6H, H-7/9/11/40/42/44), 7.27 (s, 2H, H-33/66); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ ppm: 113.9 (d, <sup>2</sup>J<sub>C-F</sub> = 21.1 Hz, C-55/57), 114.3
(d, $^2J_{CF} = 21.1$ Hz, C-48/50), 120.0 (C-23), 120.3 (C-16), 126.0 (C-63), 126.1 (C-30), 126.6 (C-42), 126.7 (C-9), 127.0 (C-34), 127.3 (C-61/65), 127.4 (C-28/32), 127.8 (C-40/44), 127.9 (C-7/11), 128.0 (C-36), 128.1 (C-2), 130.0 (C-8/10), 130.1 (C-41/43), 130.2 (C-21/25), 130.5 (C-14/18), 131.5 (C-29/31), 131.6 (C-62/64), 131.7 (C-33), 132.9 (d, $^3J_{CF} = 8.2$ Hz, C-54/58), 133.0 (d, $^3J_{CF} = 8.2$ Hz, C-47/51), 133.1 (C-22/24), 133.2 (C-15/17), 135.9 (d, $^4J_{CF} = 3.3$ Hz, C-46), 136.2 (d, $^4J_{CF} = 3.3$ Hz, C-53), [(137.8, 138.3, 138.8, 139.2, 139.3, 139.5, 139.5, 139.8, 140.2, 140.7, 140.8, 140.9, 141.0, 141.1, 141.2, 141.4), quarternary Ar-C], 160.8 (d, $^1J_{CF} = 243.8$ Hz, C-56) and 161.1 (d, $^1J_{CF} = 243.8$ Hz, C-49); $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -116.79 and -116.49; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3024 (w, Ar C–H stretch), [1601, 1573, 1510, 1489 (m, Ar C=C stretch)], 1221 (m, Ar C–F stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 253 and 280 (log $\varepsilon$ 5.19 and 4.74); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 336 nm) $\lambda_{\text{ems}}$ (nm): 363; MALDI-TOF-MS (dithranol) Calcd for C$_{66}$H$_{42}$Br$_2$F$_2$Na [M+Na]$^+$: 1055 (100%), Found: 1055 (100%).

**Dendrimer Penta-OH-Br-F (158)**

Compounds 156 (0.1082 g, 0.15 mmol, 1.0 equiv.), 143 (0.0958 g, 0.23 mmol, 1.5 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C overnight. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 9:1 to 4:1) afforded 158 (0.1557 g, 90%) as a pale yellow powder.

TLC $R_f$ = 0.28 (hexane/EtOAc = 4:1); melting point = 206-207 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 4.56 (s, 1H, OH), 6.34 (dd, 1.5 and 2.4 Hz, 1H, H-2), 6.36 (dd, 1.5 and 2.4 Hz, 1H, H-36), 6.56-6.62 (m, 4H, H-22/24/55/57), 6.63-6.70 (m, 7H, H-15/17/34/48/50/54/58), 6.72-6.79 (m, 6H, H-29/31/47/51/62/64), 6.85-6.95 (m, 6H, H-28/30/32/61/63/65), 7.02 (d, 8.6 Hz, 2H, H-21/25), 7.08-7.12 (m, 6H, H-8/10/14/18/41/43), 7.18-7.22 (m, 6H, H-7/9/11/40/42/44), 7.24 (s, 1H, H-66) and 7.25 (s, 1H, H-33); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 114.2 (d, $^2J_{CF} = 21.1$ Hz, C-48/50), 114.9 (d, $^2J_{CF} = 21.1$ Hz, C-55/57), 115.1 (C-36), 115.2 (C-2), 120.0 (C-23), 120.3 (C-16), 124.8 (C-34), 126.1 (C-63), 126.2 (C-30), 126.6 (C-42), 126.7 (C-9), 127.3 (C-61/65), 127.4 (C-28/32), 127.8 (C-40/44), 127.9 (C-7/11), 130.0 (C-8/10), 130.0 (C-41/43), 130.2 (C-21/25), 130.5 (C-14/18), 131.4 (C-29/31), 131.5 (C-62/64), 131.5 (C-66), 131.8 (C-33), 132.9 (d, $^3J_{CF} =$ 243
8.2 Hz, H-54/58), 133.0 (d, $^3J_{CF} = 8.2$ Hz, C-47/51), 133.1 (C-15/17), 133.1 (C-22/24), 135.8 (d, $^4J_{CF} = 3.3$ Hz, C-46), 136.2 (d, $^4J_{CF} = 3.3$ Hz, C-53), [(137.9, 138.5, 138.7, 139.1, 139.2, 139.3, 139.5, 139.7, 140.2, 140.4, 140.6, 140.7, 140.9, 141.0, 141.1, 141.4, 142.4, 142.6), quarternary Ar-C], 154.2 (C-1), 160.8 (d, $^1J_{CF} = 243.8$ Hz, C-56) and 161.0 (d, $^1J_{CF} = 243.8$ Hz, C-49); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -116.77 and -116.48; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3544 (w, O–H stretch), [3051, 3025 (w, Ar C–H stretch), [1592, 1510, 1489 (m, Ar C=C stretch)], 1221 (m, Ar C–F stretch), 1178 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 279 (log $\varepsilon$ 5.10 and 4.72); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 377 nm) $\lambda_{\text{ems}}$ (nm): 413, 437 and 464; MALDI-TOF-MS (dithranol) Calcd for C$_{66}$H$_{42}$Br$_2$F$_2$O $[M]^+$: 1048.2 (100%), Found: 1048.1 (100%).

6.6 Synthesis of Hexaaryl Dendrimers

6.6.1 Synthesis of Symmetrical Hexaaryl Dendrimers

_Dendrimer Hexa-H-Phenyl-Br-Br (159)_

Compounds 127 (0.2000 g, 0.7 mmol, 1.0 equiv.), 142 (1.1698 g, 2.1 mmol, 3.0 equiv.) and anhydrous $o$-xylene (4 mL) were treated as described in General Procedure E at 200 $^\circ$C for 14 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 100:0 to 99:1) and precipitation from acetone afforded 159 (0.6242 g, 66%) as a white powder. TLC $R_f$ = 0.11 (hexane/EtOAc = 99:1); melting point = $> 300^\circ$C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 6.07-6.14 (m, 4H), 6.21-6.27 (m, 3H), 6.54-6.69 (m, 13H), 6.77-6.86 (m, 14H) and 6.91-7.03 (m, 16H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: [(119.6, 119.7), C–Br], [(125.2, 125.4, 125.5, 125.6, 126.8, 126.9, 126.9, 127.1, 127.3, 129.1, 129.9, 130.0, 130.0, 131.3, 131.3, 131.4, 131.7, 132.9, 133.0, 133.0, 135.6), Ar-CH], [(138.7, 139.2, 139.5, 139.6, 139.6, 140.3, 140.3, 140.3, 140.3, 140.4, 140.4, 140.7, 140.8), quarternary Ar-C]; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3025 (w, Ar C–H stretch)], [1600, 1492 (m, Ar C=C stretch)] and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 279 (log $\varepsilon$ 5.10 and 4.72); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 377 nm) $\lambda_{\text{ems}}$ (nm): 413, 437 and 464; MALDI-TOF-MS (dithranol) Calcd for
C\textsubscript{78}H\textsubscript{50}Br\textsubscript{4}Na [M+Na]\textsuperscript{+}: 1329 (100%), Found: 1329 (100%).

**Dendrimer Hexa-H-Phenyl-F-F (160)**

Compounds 127 (27.0 mg, 0.1 mmol, 1.0 equiv.), 143 (122.0 mg, 0.3 mmol, 3.0 equiv.) and anhydrous \( o \)-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO\textsubscript{2}, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 160 (77.4 mg, 75%) as a yellow powder.

\begin{align*}
\text{TLC} & \quad R_f = 0.14 \quad \text{(hexane/EtOAc = 97.5:2.5) } \quad \text{melting point} \geq 300 \text{ °C}; \\
\text{\textsuperscript{1}H NMR} & \quad (400 MHz, CDCl\textsubscript{3}) \quad \delta \text{ ppm}: 6.12-6.17 (m, 4H), 6.22-6.30 (m, 3H), 6.52-6.58 (m, 8H), 6.62-6.76 (m, 13H), 6.80-6.89 (m, 14H), 6.92-7.03 (m, 8H); \\
\text{\textsuperscript{13}C NMR} & \quad (100 MHz, CDCl\textsubscript{3}) \quad \delta \text{ ppm}: [(113.6 (d, } \text{^2J\text{C-F} = 21.0 Hz), 113.8 (d, } \text{^2J\text{C-F} = 21.0 Hz), 125.2, 125.3, 125.4, 125.4, 126.7, 126.7, 126.8, 126.9, 127.1, 127.2, 129.1 (C-40), 131.3, 131.4, 131.5, 131.7, 132.7, 132.7, 132.8, 132.8, 132.8, 132.9, 135.8), \text{Ar-CH}], (136.6 (d, } \text{^4J\text{C-F} = 3.0 Hz), 136.8 (d, } \text{^4J\text{C-F} = 3.2 Hz), 138.8, 139.2, 139.5, 139.7, 140.5, 140.6, 140.6, 140.9), \text{quarternary Ar-C}], [(160.6 (d, } \text{^1J\text{C-F} = 243.1 Hz), 160.7 (d, } \text{^1J\text{C-F} = 243.6 Hz), C-F)]; \text{\textsuperscript{19}F NMR} & \quad (376 MHz, CDCl\textsubscript{3}) \quad \delta \text{ ppm}: -117.23, -117.23 \text{ and } -117.13; \text{\textsuperscript{FTIR} (neat)} \quad \nu_{\text{max}} (\text{cm}^{-1}): [3080, 3051 (w, Ar C–H stretch)], [1602, 1578 (m, Ar C=C stretch)] \text{ and } 1219 (m, Ar C–F stretch); \text{\textsuperscript{UV/Vis} (CH\textsubscript{2}Cl\textsubscript{2}) } \lambda_{\text{max}} (\text{nm}): 249 \text{ and } 279 (\log \varepsilon 4.95 \text{ and } 4.54); \text{\textsuperscript{Fluorescence} (CH\textsubscript{2}Cl\textsubscript{2}, } \lambda_{\text{exc}} 376 \text{ nm}) \quad \lambda_{\text{ems}} (\text{nm}): 413, 437 \text{ and } 464; \text{\textsuperscript{MALDI-TOF-MS} (dithranol) Calcd for C\textsubscript{78}H\textsubscript{50}F\textsubscript{4}Na [M+Na]\textsuperscript{+}: 1085.4 (100%), Found: 1085.6 (100%).}

**Dendrimer Hexa-OTBDMS-Phenyl-Br-Br (161)**

Compounds 128 (0.3204 g, 0.8 mmol, 1.0 equiv.), 142 (1.3008 g, 2.4 mmol, 3.0 equiv.) and anhydrous \( o \)-xylene (5 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO\textsubscript{2}, hexane/EtOAc = 100:0 to 99.4:0.6) gave 161 (0.9759 g, 86%) as a pale yellow powder.
**Experimental**

TLC $R_f = 0.19$ (hexane/EtOAc = 99:1); melting point = 255-256 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: -0.30 (s, 6H, H-79/80), 0.69 (s, 9H, H-82/83/84), 5.79 (d, 1.2 Hz, 2H, H-2/42), 6.11-6.17 (m, 4H), 6.24 (t, 1.2 Hz, 1H, H-40), 6.54-6.57 (m, 4H), 6.60-6.67 (m, 8H) and 6.77-7.03 (m, 30H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: -4.6 (C-79/80), 18.0 (C-81), 25.8 (C-82/83/84), [(119.6, 119.7), C–Br], [(121.4 (C-2/42), 125.4, 125.5, 125.7, 126.7, 126.8, 126.9, 127.0, 127.2, 127.4, 129.1 (C-40), 129.9, 130.0, 130.0, 131.2, 131.2, 131.3, 131.3, 131.6, 132.9, 133.0, 133.0), Ar-CH], [(138.6, 139.1, 139.4, 139.5, 139.6, 139.7, 140.2, 140.3, 140.4, 140.4, 140.4, 140.7, 140.8), quaternary Ar-C] and 153.2 (C-1); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3052, 3026 (w, Ar C–H stretch)], [2953, 2926, 2853 (w, sp$^3$ C–H stretch)], [1587, 1492 (m, Ar C=C stretch)], 1386 (m, sp$^3$ C–H bend), 1267, (w, Si–O stretch), 1178 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252, 279 and 300 (log $\varepsilon$ 5.11, 4.74, 4.17); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 322 nm) $\lambda_{\text{em}}$ (nm): 452; MALDI-TOF-MS (dithranol) Calcd for C$_{84}$H$_{64}$Br$_4$OSiH [M+H]$^+$: 1459 (100%), Found: 1459 (100%).

**Dendrimer Hexa-OTBDMS-Phenyl-F-F (162)**

Compounds 128 (0.4080 g, 1.0 mmol, 1.0 equiv.), 143 (1.2600 g, 3.0 mmol, 3.0 equiv.) and anhydrous o-xylene (8 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 162 (0.9845 g, 83%) as a yellow powder.

TLC $R_f = 0.19$ (hexane/EtOAc = 97.5:2.5); melting point = > 300 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: -0.30 (s, 6H, H-79/80), 0.70 (s, 9H, H-82/83/84), 5.81 (d, 1.2 Hz, 2H, H-2/42), 6.14-6.19 (m, 4H), 6.27 (t, 1.2 Hz, 1H, H-40), 6.51-6.56 (m, 8H), 6.61-6.73 (m, 12H) and 6.79-7.02 (m, 22H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: -4.6 (C-79/80), 18.0 (C-81), 25.8 (C-82/83/84), [(119.6, 119.7), C–Br], [(121.4 (C-2/42), 125.4, 125.5, 125.7, 126.7, 126.8, 126.9, 127.0, 127.2, 127.4, 129.1 (C-40), 129.9, 130.0, 130.0, 131.2, 131.2, 131.3, 131.3, 131.6, 132.9, 133.0, 133.0), Ar-CH], [(138.6, 139.1, 139.4, 139.5, 139.6, 139.7, 140.2, 140.3, 140.4, 140.4, 140.4, 140.7, 140.8), quaternary Ar-C] and 153.2 (C-1); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3052, 3026 (w, Ar C–H stretch)], [2953, 2926, 2853 (w, sp$^3$ C–H stretch)], [1587, 1492 (m, Ar C=C stretch)], 1386 (m, sp$^3$ C–H bend), 1267, (w, Si–O stretch), 1178 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252, 279 and 300 (log $\varepsilon$ 5.11, 4.74, 4.17); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 322 nm) $\lambda_{\text{em}}$ (nm): 452; MALDI-TOF-MS (dithranol) Calcd for C$_{84}$H$_{64}$Br$_4$OSiH [M+H]$^+$: 1459 (100%), Found: 1459 (100%).
Experimental

2/42), 125.3, 125.5, 126.7, 126.8, 126.9, 127.2, 127.3, 129.2 (C-40), 131.2, 131.3, 131.4, 131.7, 132.7 (d, $^3J_{C,F} = 7.4$ Hz), 132.8 (d, $^3J_{C,F} = 6.2$ Hz), 132.9 (Ar-CH), [(136.7 (d, $^4J_{C,F} = 3.0$ Hz), 136.8 (d, $^4J_{C,F} = 3.4$ Hz), 139.1, 139.2, 139.7, 139.8, 140.5, 140.6, 140.7, 140.8), quarternary Ar-CH], 153.2 (C-1), [(160.6 (d, $^1J_{C,F} = 243.1$ Hz), 160.7 (d, $^1J_{C,F} = 243.4$ Hz)), C–F]; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -117.29, -117.28 and -117.18; FTIR (neat) $\nu$max (cm$^{-1}$): [3079, 3045 (w, Ar C–H stretch)], [2960, 2931, 2858 (w, sp$^3$ C–H stretch)], [1592, 1509 (m, Ar C=C stretch)], 1393 (m, sp$^3$ C–H bend), 1250 (w, Si–O stretch), 1218 (m, Ar C–F stretch) and 1196 (w, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda$max (nm): 249, 275 and 298 (log $\varepsilon$ 5.11, 4.69 and 4.05); Fluorescence (CH$_2$Cl$_2$, $\lambda_{exc}$ 322 nm) $\lambda_{ems}$ (nm): 351 and 398; MALDI-TOF-MS (dithranol) Calcd for C$_{84}$H$_{64}$F$_4$OSiNa [M+Na]$^+$: 1215.5 (100%), Found: 1215.5 (100%).

Dendrimer Hexa-OH-Phenyl-Br-Br (163)

Synthesis of this compound was carried out in two experiments with the same method described in General Procedure B. The only difference was the use of Et$_2$O during extraction in the second experiment rather than CH$_2$Cl$_2$ in the first one. The extraction solvent was changed in order to avoid the formation of several unwanted by-products that formed when CH$_2$Cl$_2$ was used as the solvent.

Using CH$_2$Cl$_2$ as solvent during extraction work-up

Dendrimer 161 (0.2513 g, 0.17 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 0.34 mL, 0.34 mmol, 2.0 equiv.) and anhydrous THF (3 mL) were treated as described in General Procedure B. However, instead of diethyl ether, CH$_2$Cl$_2$ was used during extraction work-up. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 9:1 to 4:1) afforded 163 (0.0843 g, 36%) as a pale yellow powder and a mixture of by-products. The by-products were subjected to another flash column chromatography purification (SiO$_2$, hexane/EtOAc = 95:5) to give 174 (0.0667 g, 29%) and 175 (0.0647 g, 14%) both obtained as pale yellow powders.

Using Et$_2$O as solvent during extraction work-up

Dendrimer 161 (0.2874 g, 0.2 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 0.24 mL, 0.24 mmol, 1.2 equiv.) and anhydrous THF (5 mL) were treated as described in General Procedure B. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 9:1 to 4:1) afforded 163 (0.2536 g, 96%) as a pale yellow powder.
Experimental

Product 163 data from both methods:

TLC $R_f = 0.23$ (hexane/EtOAc = 4:1); melting point = 228 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 3.87 (s, 1H, OH), 5.74 (d, 1.2 Hz, 2H, H-2/42), 6.10-6.15 (m, 4H), 6.24 (t, 1.2 Hz, 1H, H-40), 6.54-6.69 (m, 12H) and 6.78-7.04 (m, 30H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 116.4 (C-2/42), [(119.7, 119.8), C–Br], [(125.5, 125.5, 125.7, 126.8, 126.9, 127.0, 127.2, 127.4, 128.9 (C-40), 129.9, 130.0, 130.1, 131.2, 131.5, 132.9, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, Ar-CH], [(138.8, 139.1, 139.1, 139.4, 139.5, 140.1, 140.1, 140.2, 140.2, 140.3, 140.3, 140.7, 140.7), quarternary Ar-C] and 153.1 (C-1); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3557 (w, O–H stretch), [3053, 3025 (w, Ar C–H stretch)], [1591, 1492 (m, Ar C=C stretch)], 1172 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252, 279 and 300 (log $\varepsilon$ 5.02, 4.66 and 4.12); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 414 and 436; MALDI-TOF-MS (dithranol) Calcd for C$_{78}$H$_{50}$Br$_4$ONa [M+Na]$^+$: 1345 (100%), Found: 1345 (100%).

By-product 174 data:

TLC $R_f = 0.31$ (hexane/EtOAc = 9:1); melting point = > 300 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 4.66 (d, $^2$$J_{H-F}$ = 55.0 Hz, 2H, H-79), 6.03 (d, 1.6 Hz, 2H, H-2/42), 6.09-6.14 (m, 4H), 6.39 (t, 1.6 Hz, 1H, H-40), 6.55-6.69 (m, 12H) and 6.80-7.06 (m, 30H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 101.8 (d, $^1$$J_{C-F}$ = 216.3 Hz, C-79), 118.5 (C-2/42), [(119.7, 119.8), C–Br], [(125.5, 125.5, 125.7, 126.8, 126.9, 127.0, 127.1, 127.2, 127.4, 130.0, 130.1, 131.2, 131.3, 131.4, 131.6, 132.9, 132.9, 132.9, 133.0, Ar-CH], [(138.9, 138.9, 139.2, 139.4, 139.5, 140.1, 140.1, 140.2, 140.2, 140.3, 140.3, 140.3, 140.7, 140.8), quarternary Ar-C] and 155.3 (d, $^3$$J_{C-F}$ = 3.4 Hz, C-1); $^{19}$F NMR (376 MHz, $^1$H-coupled, CDCl$_3$) δ ppm: -146.06 (t, $^2$$J_{H-F}$ = 55.0 Hz); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3025 (w, Ar C–H stretch)], [1589, 1491 (m, Ar C=C stretch) and 1189 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 281 (log $\varepsilon$ 5.09 and 4.70); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 437 and 464; MALDI-TOF-MS (dithranol)
Calcd for C_{79}H_{51}Br_{4}FONa [M+Na]^+: 1377 (100%), Found: 1377 (100%).

**By-product 175 data:**

**TLC** R_f = 0.21 (hexane/EtOAc = 9:1); **melting point** = 272-273 °C; **^1H NMR** (400 MHz, CDCl_3) δ ppm: 3.66 (s, 2H, H-79), 5.78 (d, 1.6 Hz, H-2/42/81/121), 6.07-6.13 (m, 8H), 6.23 (t, 1.6 Hz, H-40/119), 6.55-6.74 (m, 32H) and 6.80-7.00 (m, 52H); **^13C NMR** (100 MHz, CDCl_3) δ ppm: 94.6 (C-79), 118.4 (C-2/42/81/121), [(119.7, 119.8), C–Br], [(125.4, 125.5, 126.7, 126.8, 126.9, 127.1, 127.4, 130.0, 130.1, 130.1, 131.2, 131.2, 131.3, 131.3, 131.5, 132.8, 132.9, 133.0), Ar-CH], [(138.8, 139.1, 139.3, 139.4, 139.5, 140.2, 140.4, 140.7), quartenary Ar-C] and 156.0 (C-1/80); **FTIR** (neat) ν_max (cm^{-1}): [3054, 3025 (w, Ar C–H stretch)], [1585, 1491 (m, Ar C=C stretch), 1179 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); **UV/Vis** (CH_2Cl_2) λ_max (nm): 252, 281 and 299 (log ε 5.51, 5.08 and 4.52); **Fluorescence** (CH_2Cl_2, λ_{exc} 376 nm) λ_{ems} (nm): 413, 437 and 464; **MALDI-TOF-MS** (DCTB) Calcd for C_{157}H_{100}Br_{8}O_2 [M]^+: 2658.1 (100%), Found: 2657.1 (100%).

**Dendrimer Hexa-OH-Phenyl-F-F (164)**

Compound 162 (0.3576 g, 0.30 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 0.36 mL, 0.36 mmol, 3.0 equiv.) and anhydrous THF (6 mL) were treated as described in General Procedure B. Purification by flash column chromatography (SiO_2, hexane/EtOAc = 9:1 to 4:1) afforded 164 (0.2986 g, 92%) as a pale yellow powder.

**TLC** R_f = 0.23 (hexane/EtOAc = 4:1); **melting point** = 200 °C (decomposition); **^1H NMR** (400 MHz, CDCl_3) δ ppm: 5.76 (d, 1.2 Hz, 2H, H-2/42), 6.13-6.16 (m, 4H), 6.27 (t, 1.2 Hz, 1H, H-40), 6.51-6.57 (m, 8H), 6.61-6.74 (m, 12H) and
Experimental

6.82-7.04 (m, 22H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(113.7 (d, $^2$J$_{C-F}$ = 21.0 Hz), 113.8 (d, $^2$J$_{C-F}$ = 21.0 Hz), 116.4 (C-242), 125.3, 125.5, 125.6, 126.7, 126.8, 126.8, 126.9, 127.2, 127.3, 129.0 (C-40), 131.3, 131.3, 131.6, 132.7, 132.7, 132.8, 132.9), Ar-CH], [(136.6 (d, $^4$J$_{C-F}$ = 3.5 Hz), 136.7 (d, $^4$J$_{C-F}$ = 3.5 Hz), 138.9, 139.3, 139.7, 140.2, 140.4, 140.5, 140.6, 140.8), quarternary Ar-C], 153.1 (C-1), [(160.6 (d, $^1$J$_{C-F}$ = 243.5 Hz), 160.7 (d, $^1$J$_{C-F}$ = 243.1 Hz), C–F]; $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -117.18, -117.17 and -117.08; FTIR (neat) $\nu$$_{\text{max}}$ (cm$^{-1}$): 3565 (w, O–H stretch), [3053, 3025 (w, Ar C–H stretch)], [1593, 1510 (m, Ar C=C stretch)], 1222 (m, Ar C–F stretch) and 1177 (w, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda$$_{\text{max}}$ (nm): 249, 276 and 300 (log $\varepsilon$ 5.02, 4.61 and 4.01); Fluorescence (CH$_2$Cl$_2$, $\lambda$$_{\text{exc}}$ 376 nm) $\lambda$$_{\text{ems}}$ (nm): 414, 435 and 463; MALDI-TOF-MS (dithranol) Calcd for C$_{78}$H$_{50}$F$_4$ONa [M+Na]$^+$: 1101.4 (100%), Found: 1101.2 (100%).

Dendrimer Hexa-H-(2-Pyridyl)-Br-Br (165)

Compounds 129 (0.0140 g, 0.5 mmol, 1.0 equiv.), 142 (0.8130 g, 1.5 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 5 d. The resulting mixture was added dropwise into EtOH (100 mL) and cooled to 0 °C using an ice bath for an hour. The precipitate formed was collected by filtration under vacuum and washed with cold EtOH. The crude product was then recrystallised from hexane to obtain 165 (0.2124 g, 32%) as a pale brown powder.

TLC $R_f$ = 0.63 (hexane/EtOAc = 1:1); melting point = 216-217 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 5.26 (br s, 1H), 5.41 (br d, 5.6 Hz, 1H), 6.09-7.01 (br m, 43H), 7.99 (br s, 1H) and 8.17 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 119.7, 119.8, 120.3 (br), 125.5 (br), 125.8 (br), 126.1 (br), 126.9 (br), 127.1 (br), 129.9 (br), 130.0 (br), 130.3 (br), 131.4 (br), 131.6 (br), 132.7 (br), 132.9 (br), 134.9 (br), 138.6, 138.9, 139.2 (br), 139.6 (br), 140.1 (br), 140.4 (br), 147.7 (br) and 147.9 (br); FTIR (neat) $\nu$$_{\text{max}}$ (cm$^{-1}$): [3053, 3022 (w, Ar C–H stretch)], [1587, 1488, 1471 (m, Ar C=C and C=N stretch)] and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda$$_{\text{max}}$ (nm): 251 and 279 (log $\varepsilon$ 4.91 and 4.56); Fluorescence (CH$_2$Cl$_2$, $\lambda$$_{\text{exc}}$ 376 nm) $\lambda$$_{\text{ems}}$ (nm): 414, 435 and 463; MALDI-TOF-MS (dithranol)
Calcd for C_{76}H_{48}Br_{4}N_{2}H [M+H]^+: 1309 (100%), Found: 1309 (100%).

Dendrimer Hexa-OMEM-(2-Pyridyl)-Br-Br (166)

Compounds 130 (0.0500 g, 0.13 mmol, 1.0 equiv.), 142 (0.2117 g, 0.39 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 5 d. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 4:1 to 0:1) to remove most of the impurities. Other impurities failed to be removed, hence, crude 166 (0.1544 g, 84%) was obtained as a yellow powder.

TLC Rf = 0.33 (hexane/EtOAc = 1:1); melting point = 217-218 °C; 1H NMR (400 MHz, CDCl₃) δ ppm: 3.25-3.27 (br m, 8H), 4.32 (br s, 2H), 5.30 (br s, 1H), 5.45 (br s, 1H), 6.00 (br s, 2H), 6.23-7.04 (br m, 50H), 8.03 (br s, 1H) and 8.20 (br s, 1H); 13C NMR (100 MHz, CDCl₃) δ ppm: 59.0, 60.5, 63.0, 71.5, 89.0, 119.7, 122.8, 123.6, 125.5, 125.9, 126.9, 127.0 (br), 127.1, 127.2, 130.0 (br), 132.7 (br) and 132.8 (br); FTIR (neat) νmax (cm⁻¹): [3054, 3024 (w, Ar C–H stretch)], [2961, 2889, 2813 (w, sp³ C–H stretch), [1587, 1488, 1471 (m, Ar C=C and C=N stretch)], 1386 (m, sp³ C–H bend), 1188 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH₂Cl₂) λmax (nm): 251, 278 and 300 (log ε 5.07, 4.73 and 4.18); Fluorescence (CH₂Cl₂, λexc 373 nm) λems (nm): 413, 438 and 465; MALDI-TOF-MS (dithranol) Calcd for C_{80}H_{57}Br_{4}N_{2}O_{3} [M+H]^+: 1413 (100%), Found: 1413 (100%).

Dendrimer Hexa-OH-(2-Pyridyl)-Br-Br (167)

Through Deprotection Reaction of 166

Compounds 166 (0.0518 g, 0.04 mmol) and CH₂Cl₂ (1 mL) were added into a 5 mL round bottom flask and stirred. Anhydrous ZnBr₂ (0.0900 g, 0.4 mmol, 10 equiv.) was then added into the solution and the reaction mixture was stirred at room temperature. The reaction was judged to be complete after no more starting material was observed by TLC analysis. The resulting mixture was then washed with saturated NaHCO₃ and brine, dried over MgSO₄ and concentrated. The residue was then purified by flash column chromatography (SiO₂, toluene/acetonitrile = 5:1) to give 167 (0.0154 g, 32%) as a yellow powder.
Experimental

Through Diels-Alder Cycloaddition Reaction

Compounds 131 (0.0720 g, 0.24 mmol, 1.0 equiv.), 142 (0.3955 g, 0.72 mmol) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 175 °C for 3 d. Purification by flash column chromatography (SiO₂, hexane/acetone = 5:1 to 3:1) afforded 167 (0.3208 g, 78%) as a yellow powder.

Data for both methods:

TLC Rf = 0.13 (toluene/acetone = 5:1) and 0.20 (hexane/acetone = 2:1); melting point = > 165-166 °C (decomposition);

1H NMR (400 MHz, CDCl₃) δ ppm: 5.83 (s, 2H), 6.09 (s, 1H), 6.31-7.12 (m, 57H), 7.82 (br s, 1H);

13C NMR (100 MHz, CDCl₃) δ ppm: 118.7, 118.8, 122.1, 127.2, 128.0, 129.0, 131.6, 133.8, 138.0 and 139.2; FTIR (neat) νmax (cm⁻¹): [3054, 3026 (w, Ar C–H stretch)], [1585, 1488 (m , Ar C=C and C=N stretch)], 1180 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); MALDI-TOF-MS (dithranol) Calcd for C₇₆H₄₉Br₄N₂O [M+H]+: 1325 (100%), Found: 1325 (100%).

Dendrimer Hexa-H-(4-Fluorophenyl)-Br-Br (168)

Compounds 132 (0.1000 g, 0.32 mmol, 1.0 equiv.), 142 (0.5178 g, 0.96 mmol) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 168 (0.2983, 70%) as a white powder.

TLC Rf = 0.14 (hexane/EtOAc = 97.5:2.5); melting point = > 300 °C;

1H NMR (400 MHz, CDCl₃) δ ppm: 5.65 (ddd, 2.4, 5.6 and 8.3 Hz, 1H), 6.08-6.14 (m, 2H), 6.24-6.32 (m, 3H), 6.41-6.46 (m, 1H), 6.49-6.69 (m, 18H), 6.73-6.78 (m, 2H), 6.85-6.86 (m, 8H), 6.93-7.06 (m, 12H) and 7.06-7.13 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ ppm: [113.6 (d, 2J_C-F = 23.0 Hz), 114.1 (d, 2J_C-F = 23.1 Hz)], Ar-CH], [(119.7, 119.8), C–Br], [(125.5, 125.6, 125.7, 125.9, 127.0, 127.0, 127.1,
127.1, 127.3, 127.3, 129.1, 129.2, 129.9, 130.0, 130.1, 131.1, 131.2, 131.3, 131.6, 131.6, 132.6, 132.6, 132.7, 132.8, 132.9, 133.0, 133.1 (d, $^3J_{C,F} = 8.0$ Hz), 133.2 (d, $^3J_{C,F} = 7.9$ Hz), 135.5), Ar-CH], [(136.2 (d, $^4J_{C,F} = 3.4$ Hz), 136.5 (d, $^4J_{C,F} = 3.0$ Hz), 138.7, 138.7, 138.8, 139.3, 139.4, 139.5, 139.6, 139.7, 139.7, 139.9, 140.1, 140.1, 140.2, 140.3, 140.4, 140.8, 141.0), quarternary Ar-C], [160.6 (d, $^1J_{C,F} = 242.9$ Hz) 160.8 (d, $^1J_{C,F} = 243.2$ Hz), C–F], $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ ppm: -117.03 and -116.67; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3045, 3031 (w, Ar C–H stretch)], [1600, 1508, 1492 (m, Ar C=C stretch), 1219 (m, Ar C–F stretch) and 1073 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 250 and 278 (log $\varepsilon$ 5.06 and 4.72); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 428 and 441; MALDI-TOF-MS (DCTB) Calcd for C$_{78}$H$_{48}$Br$_4$F$_2$ [M]$^+$: 1342.0 (100%), Found: 1342.1 (100%).

**Dendrimer Hexa-H-(4-Fluorophenyl)-F-F (169)**

Compounds 132 (0.1000 g, 0.32 mmol, 1.0 equiv.), 142 (0.5178 g, 0.96 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 $^\circ$C for 14 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 169 (0.3178 g, 91%) as a white powder.

**TLC $R_f$** = 0.08 (hexane/EtOAc = 97.5:2.5); melting point $>$ 300 $^\circ$C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 5.68 (ddd, 2.4, 5.6 and 8.3 Hz, 1H), 6.11-6.17 (m, 2H), 6.26-6.34 (m, 3H), 6.42-6.47 (m, 1H), 6.51-6.74 (m, 26H), 6.76-6.81 (m, 2H), 6.84-6.89 (m, 8H), 6.94-7.05 (m, 4H) and 7.09-7.13 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: [(113.6 (d, $^2J_{C,F} = 24.1$ Hz), 113.7 (d, $^2J_{C,F} = 21.2$ Hz), 113.8 (d, $^2J_{C,F} = 21.1$ Hz), 114.1 (d, $^2J_{C,F} = 23.1$ Hz), 125.5, 125.5, 125.6, 125.8, 126.9, 127.0, 127.0, 127.1, 127.2, 127.3, 129.1, 129.2, 131.2, 131.3, 131.3, 131.3, 131.7, 131.7, 132.5, 132.6, 132.7, 132.8, 132.8, 132.9, 133.2, 133.3, 133.3, 135.6), Ar-CH], [(136.3 (d, $^4J_{C,F} = 3.3$ Hz), 136.5 (d, $^4J_{C,F} = 3.3$ Hz), 136.5 (d, $^4J_{C,F} = 3.7$ Hz), 136.6 (d, $^4J_{C,F} = 3.1$ Hz), 136.7 (d, $^4J_{C,F} = 3.5$ Hz), 138.8, 138.9, 139.4, 139.5, 139.7, 140.1, 140.1, 140.4, 140.4, 140.5, 140.6, 140.8, 140.9, 141.1), quarternary Ar-C], [(160.6 (d, $^1J_{C,F} = 242.3$ Hz), 160.7 (d, $^1J_{C,F} = 243.5$ Hz), 160.7 (d, $^1J_{C,F} = 243.8$ Hz), 160.8 (d, $^1J_{C,F} = 243.0$ Hz)), C–F]; $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ ppm: -117.18, -117.05, -117.04, -116.93, -116.93 and -116.80; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3052 (w, Ar C–H stretch), [1602
Experimental

(m), 1510 (s (Ar C=C stretch)] and 1220 (s, Ar C–F stretch); UV/Vis (CH₂Cl₂) \( \lambda_{\text{max}} \) (nm): 249 and 276 (log \( \varepsilon \) 5.04 and 4.65); Fluorescence (CH₂Cl₂, \( \lambda_{\text{exc}} \) 376 nm) \( \lambda_{\text{ems}} \) (nm): 409, 441 and 459; MALDI-TOF-MS (DCTB) Calcd for C_{78}H_{48}F_{6} [M]^+: 1098.4 (100%), Found: 1098.4 (100%).

Dendrimer Hexa-OH-(4-Fluorophenyl)-Br-Br (170)

Compounds 133 (0.0990 g, 0.3 mmol, 1.0 equiv.), 142 (0.4878 g, 0.9 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 21 d. Purification by reverse-phase HPLC (ACN/H₂O = 90:10 to 100:0) afforded 170 (0.3018 g, 74%) as a pale yellow powder.

\[ \text{TLC} \text{ R}_f = 0.28 \text{ (hexane/EtOAc = 4:1); } \text{melting point} = 260 \, ^\circ \text{C} \text{ (decomposition); } ^1\text{H NMR} \text{ (400 MHz, CDCl}_3 \delta \text{ ppm: [113.7 (d, }^2\text{J}_{\text{C-F}} = 21.1 \text{ Hz), 113.9 (d, }^2\text{J}_{\text{C-F}} = 20.9 \text{ Hz), 114.0 (d, }^2\text{J}_{\text{C-F}} = 21.1 \text{ Hz), 114.2 (d, }^2\text{J}_{\text{C-F}} = 20.9 \text{ Hz), 116.5, 116.5), Ar-CH], [(119.8, 119.9), C–Br), [125.7, 125.7, 125.8, 126.0, 127.0, 127.0, 127.0, 127.1, 127.2, 127.2, 127.3, 127.5, 128.7, 128.7, 130.0, 130.0, 130.1, 131.1, 131.2, 131.2, 131.2, 131.5, 131.5, 132.4, 132.5, 132.5, 132.6, 132.7, 132.8, 132.9, 133.0, 133.0, 133.1, 133.1), Ar-CH], [(136.1 (d, }^4\text{J}_{\text{C-F}} = 3.5 \text{ Hz), 136.4 (d, }^4\text{J}_{\text{C-F}} = 3.4 \text{ Hz), 139.0, 139.1, 139.3, 139.4, 139.5, 139.6, 139.7, 140.0, 140.1, 140.1, 140.1, 140.2, 140.3, 140.3, 140.8, 141.0), quarternary Ar-C], [(153.3, 153.3), C–O], [(160.7 (d, }^1\text{J}_{\text{C-F}} = 243.0 \text{ Hz), 160.8 (d, }^1\text{J}_{\text{C-F}} = 243.6 \text{ Hz)), C–F]]; ^19\text{F NMR} \text{ (470 MHz, CDCl}_3 \delta \text{ ppm: -116.76 and -116.48; } \text{FTIR} \text{ (neat) } \nu_{\text{max}} \text{ (cm}^{-1} \text{): 3563 (w, O–H stretch), [3054, 3026 (w, Ar C–H stretch), [1591, 1508, 1492 (m, Ar C=C stretch), [1221 (m, Ar C–F stretch), 1177 (w, C–O stretch) and 1072 (s, Ar C–Br stretch); UV/Vis (CH₂Cl₂) }\lambda_{\text{max}} \text{ (nm): 251, 277 and 299 (log }\varepsilon\text{ 5.10, 4.72 and 4.19); Fluorescence (CH₂Cl₂, }\lambda_{\text{exc}} \text{ 376 nm) }\lambda_{\text{ems}} \text{ (nm): 417, 433 and 463; MALDI-TOF-MS} \text{ (DCTB) Calcd for C}_{78}\text{H}_{48}\text{Br}_{6}\text{F}_{2}\text{O [M]}^+: 1358.0 (100%), Found: 1358.1 (100%).} \]
**Experimental**

**Dendrimer Hexa-H-(2-Fluorophenyl)-Br-Br (171)**

Compounds 134 (0.1000 g, 0.32 mmol, 1.0 equiv.), 142 (0.5178 g, 0.96 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 171 (0.3913 g, 92%) as a pale yellow powder.

TLC $R_f = 0.10$ (hexane/EtOAc = 97.5:2.5); melting point = > 300 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 5.32 ($d$, 7.6 Hz, 2H), 5.38 ($d$, 7.7 Hz, 2H), 5.43 ($d$, 7.5 Hz, 4H), 5.48 ($td$, 1.6 and 7.5 Hz, 2H), 6.03 ($td$, 1.6 and 7.5 Hz, 3H), 6.12 ($d$, 7.5 Hz, 3H), 6.18 ($td$, 1.6 and 7.4 Hz, 3H), 6.23-7.15 ($m$, 36H) and 7.18-7.22 ($m$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(113.9, 113.9, 114.1, 114.1, 114.1, 114.2, 114.3, 114.4, 114.5, 114.6, 114.7, 114.8, 115.0, 119.7, 119.8, 119.8, 119.9, 122.9, 123.1, 123.1, 123.2, 123.2, 125.2, 125.3, 125.4, 125.4, 125.6, 125.7, 125.7, 125.8, 125.8, 125.9, 126.1, 126.1, 126.2, 126.3, 126.6, 126.6, 126.7, 126.7, 127.0, 127.0, 127.1, 127.1, 127.2, 127.2, 127.3, 127.3, 127.4, 127.5, 127.9, 128.0, 128.2, 128.2, 128.3, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 128.8, 129.0, 129.1, 129.1, 129.1, 129.3, 129.3, 129.4, 129.8, 129.9, 130.0, 130.1, 130.1, 130.3, 130.3, 130.4, 130.5, 130.6, 130.6, 130.7, 130.7, 130.8, 130.8, 130.9, 130.9, 131.0, 131.0, 131.2, 131.4, 131.6, 131.7, 131.8, 131.8, 131.9, 132.0, 132.2, 132.2, 132.7, 132.8, 132.8, 132.9, 133.0, 133.0, 133.1, 133.4, 133.5, 134.3, 134.5, 134.5, 134.6, 134.6, 134.7), Ar-CH], [(138.0, 138.1, 138.2, 138.5, 138.6, 138.6, 138.7, 138.7, 138.8, 138.8, 138.8, 138.9, 138.9, 139.2, 139.2, 139.3, 139.4, 139.4, 139.5, 139.5, 139.6, 139.6, 139.7, 139.7, 139.7, 139.8, 139.8, 139.9, 139.9, 139.9, 140.0, 140.1, 140.1, 140.2, 140.2, 140.3, 140.4, 140.4, 140.5, 140.5, 140.6, 140.6, 140.7, 140.8, 140.8, 141.4, 141.5, 141.5, 141.6, 141.7), quarternary Ar-C], [(158.4, 158.6, 158.7, 158.8, 160.8, 160.9, 160.9, 160.9, 161.0), C–F]; $^{19}$F NMR (470 MHz, CDCl$_3$) δ ppm: -112.64, -112.16, -112.16, -111.86, -110.10, -110.87, -110.63 and -110.53; FTIR (neat) $\nu_{max}$ (cm$^{-1}$): [3082, 3052, 3027 (w, Ar C–H stretch)], [1601, 1580, 1492 (m, Ar C=C stretch)], 1229 (m, Ar C–F stretch) and 1073 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{max}$ (nm): 250 and 280 (log $\varepsilon$ 5.06 and 4.64); Fluorescence (CH$_2$Cl$_2$, $\lambda_{exc}$ 376 nm) $\lambda_{ems}$ (nm): 414, 437 and 464; MALDI-TOF-MS (dithranol) Calcd for C$_{78}$H$_{48}$Br$_4$F$_2$Na [M+Na]$^+$: 1365.0 (100%), Found: 1365.0 (100%).
**Experimental**

*Dendrimer Hexa-H-(2-Fluorophenyl)-F-F (172)*

Compounds 134 (0.1000 g, 0.32 mmol, 1.0 equiv.), 143 (0.4013 g, 0.96 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO\(_2\), hexane/EtOAc = 100:0 to 99.4:0.6) afforded 172 (0.2914 g, 83%) as a white powder.

TLC \( R_f = 0.08 \) (hexane/EtOAc = 97.5:2.5); melting point = > 300 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 5.34 (\( d, 7.8 \) Hz, 2H), 5.39-5.46 (\( m, 6H \)), 5.50 (\( td, 1.6 \) and 7.5 Hz, 2H), 6.04 (\( td, 1.3 \) and 7.4 Hz, 3H), 6.14 (\( d, 7.6 \) Hz, 3H), 6.19-6.36 (\( m, 22H \)), 6.39-6.44 (\( m, 8H \)), 6.48-7.15 (\( m, 335H \)) and 7.18-7.22 (\( m, 3H \)); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: [(113.6, 113.6, 113.7, 113.7, 113.8, 113.8, 113.9, 114.0, 114.0, 114.1, 114.1, 114.3, 114.3, 114.4, 114.5, 114.5, 114.6, 114.6, 114.7, 114.8, 115.0, 115.0, 122.9, 122.9, 123.1, 123.1, 123.1, 123.2, 123.2, 123.2, 123.3, 125.1, 125.1, 125.2, 125.3, 125.4, 125.5, 125.5, 125.6, 125.6, 125.7, 125.7, 125.9, 126.1, 126.2, 126.3, 126.5, 126.6, 126.9, 126.9, 127.0, 127.0, 127.1, 127.1, 127.2, 127.2, 127.3, 127.3, 127.4, 127.4, 127.9, 128.0, 128.1, 128.2, 128.2, 128.8, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.9, 129.0, 129.1, 129.2, 129.3, 129.4, 129.4, 129.4, 129.5, 129.9, 130.4, 130.5, 130.6, 130.7, 130.7, 130.8, 130.8, 130.9, 131.0, 131.2, 131.3, 131.3, 131.4, 131.7, 131.7, 131.7, 131.8, 131.8, 131.8, 131.9, 132.0, 132.0, 132.1, 132.3, 132.3, 132.6, 132.6, 132.6, 132.7, 132.7, 132.8, 132.8, 132.8, 132.9, 132.9, 132.9, 133.0, 133.1, 133.2, 133.6, 133.7, 133.7, 133.7, 134.1, 134.2, 134.3, 134.4, 134.5, 134.6, 134.7), Ar-CH], [(136.3, 136.4, 136.4, 136.4, 136.5, 136.5, 136.5, 136.6, 136.6, 136.6, 136.7, 136.7, 136.7, 136.7, 136.7, 136.8, 138.1, 138.3, 138.4, 138.6, 138.7, 139.0, 139.0, 139.2, 139.2, 139.2, 139.2, 139.3, 139.3, 139.4, 139.4, 139.4, 139.7, 139.9, 140.0, 140.0, 140.1, 140.2, 140.3, 140.3, 140.4, 140.4, 140.5, 140.5, 140.6, 140.7, 140.7, 140.7, 140.8, 140.9, 141.0, 141.5, 141.5, 141.5, 141.7, 141.7, 141.9), quarternary Ar-C]), [(158.5, 158.5, 158.6, 158.7, 159.5, 159.5, 160.9, 161.0, 161.1, 161.1, 161.9, 162.0), C–F]; \(^1^9\)F NMR (470 MHz, CDCl\(_3\)) \( \delta \) ppm: -117.18, -117.13, -117.12, -117.09, -117.06, -117.05, -117.04, -117.02, -117.01, -116.99, -116.97, -116.96, -116.96, -112.66, -112.18, -112.16, -111.86, -111.10, -110.61 and -110.52; FTIR (neat) \( \nu_{\text{max}} \) (cm\(^{-1}\)): [3050, 3028 (w, Ar C–H stretch)], [1603 (m), 1510 (s) (Ar C=C stretch)] and 1226 (s, Ar C–F stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \( \lambda_{\text{max}} \) (nm): 247 and 276 (log \( \varepsilon \) 5.03 and 4.62); Fluorescence (CH\(_2\)Cl\(_2\), \( \lambda_{\text{exc}} \) 376 nm) \( \lambda_{\text{ems}} \) (nm): 413, 437 and 465; MALDI-TOF-MS (dithranol)
Experimental

Calcd for C_{78}H_{48}F_{6} [M+H]^+: 1121 (100%), Found: 1121 (100%)

Dendrimer Hexa-OH-(2-Fluorophenyl)-Br-Br (173)

Compounds 135 (0.0990 g, 0.3 mmol, 1.0 equiv.), 142 (0.4878 g, 0.9 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E 200 °C for 21 d. Purification by reverse-phase HPLC (ACN/H_2O = 90:10 to 100:0) afforded 173 (0.3588 g, 88%) as a yellow powder.

TLC R_f = 0.18 (hexane/EtOAc = 4:1); melting point = 248-249 °C; ^1H NMR (400 MHz, CDCl_3) δ ppm: 3.83-3.90 (m, 4H, OH), 5.37 (d, 7.7 Hz, 1H), 5.42 (d, 7.8 Hz, 1H), 5.46 (d, 7.0 Hz, 2H), 5.52 (td, 1.6 and 7.5 Hz, 1H), 5.73-5.75 (m, 3H), 5.79-5.80 (m, 1H), 5.87 (d, 1.1 Hz, 1H), 5.90 (d, 1.3 Hz, 1H), 5.98-5.99 (m, 1H), 6.04 (td, 1.4 and 7.5 Hz, 1H), 6.13 (d, 7.7 Hz, 1H), 6.18-6.23 (m, 3H), 6.30 (d, 7.6 Hz, 1H), 6.37-6.38 (m, 1H), 6.42-7.16 (m, 168H) and 7.16-7.24 (m, 1H); ^13C NMR (100 MHz, CDCl_3) δ ppm: [111.9, 111.9, 112.0, 112.1, 114.4, 114.6, 114.6, 114.8, 115.5, 115.7, 116.0, 118.3, 118.7, 120.0, 122.3, 122.7, 122.9, 122.9, 123.1, 123.1, 124.0, 124.1, 125.7, 126.0, 126.1, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3, 127.3, 127.4, 127.9, 128.1, 128.8, 128.8, 128.9, 130.0, 130.1, 130.2, 130.3, 130.3, 130.4, 130.5, 130.8, 131.0, 131.0, 131.1, 131.2, 132.4, 132.4, 132.7, 132.7, 132.9, 132.9, 132.9, 133.0, 133.0, 133.3, 133.5, 133.5, 134.9, 135.0), Ar-CH] [(139.1, 139.1, 139.3, 139.5, 139.5, 139.6, 139.6, 139.7, 140.2, 140.2, 140.4, 141.3, 141.4, 141.8, 141.9), quaternary Ar-C] [(153.9, 154.2), C–O], [(158.2, 158.2, 158.3, 161.3, 161.3 161.5), C–F]; ^19F NMR (470 MHz, CDCl_3) δ ppm: -112.58, -112.08, -112.07, -111.80, -111.08, -110.86, -110.56 and -110.49; FTIR (neat) υ_max (cm⁻¹): 3571 (w, O–H stretch), [3081, 3055, 3025 (w, Ar C–H stretch)], [1591, 1491 (m, Ar C=C stretch), 1228 (m, Ar C–F stretch), 1174 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH_2Cl_2) λ_max (nm): 250, 278 and 300 (log ε 5.09, 4.62 and 4.07); Fluorescence (CH_2Cl_2, λ_exc 376 nm) λ_em (nm): 413, 437 and 464; MALDI-TOF-MS (DCTB) Calcd for C_{78}H_{48}Br_4F_2O [M]^+: 1358.0 (100%), Found: 1358.0 (100%).
6.6.2 Synthesis of Hexaaryl Dendrimer Monoadducts

Monoadduct MonoHexa-H-Phenyl-Br (178)

Compounds 142 (69.0 mg, 0.13 mmol, 1.0 equiv.) 127 (43.0 mg, 0.15 mmol, 1.2 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 100:0 to 99.4:0.6) afforded 178 (28.7 mg, 29%) as a yellow powder.

TLC Rf = 0.25 (hexane/EtOAc = 97.5:2.5); melting point = 172-173 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: 6.69-6.71 (m, 4H), 6.77-6.96 (m, 17H), 7.01-7.05 (m, 6H), 7.30-7.33 (m, 6H), 7.42-7.45 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ppm: 88.7 (C-44), 89.7 (C-43), [(119.9, 121.8, 123.5, 125.7, 125.9, 126.9, 126.9, 127.0, 127.0, 127.1, 127.2, 128.2, 128.4, 128.9, 130.2, 131.2, 131.3, 131.4, 131.6, 133.0, 133.0, 134.6), Ar-CH], [(139.0, 139.2, 139.3, 139.4, 139.8, 140.0, 140.1, 140.1, 140.5, 140.6, 141.0), quarternary Ar-C]; FTIR (neat) υmax (cm⁻¹): [3079, 3055, 3024 (w, Ar C–H stretch)], [1600, 1579, 1491 (m, Ar C=C stretch)] and 1071 (m, Ar C–Br stretch); UV/Vis (CH₂Cl₂) λmax (nm): 250, 283 and 302 (log ε 4.86, 4.71 and 4.48); Fluorescence (CH₂Cl₂, λexc 354 nm) λems (nm): 413, 438 and 464; HRMS Calcd for C₅₀H₃₂Br₂ [M]⁺ (monoisotopic): 791.0949, Found: 791.0947.

Monoadduct MonoHexa-OTBDMS-Phenyl-Br (179)

Compounds 142 (0.9030 g, 0.17 mmol, 1.0 equiv.), 128 (0.1020 g, 0.25 mmol, 1.5 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by preparative TLC (SiO₂, hexane/Et₂O = 97:3) afforded 179 (0.0701 g, 46%) as a pale yellow powder.

TLC Rf = 0.30 (hexane/Et₂O = 97:3); melting point = 165-166 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: -0.06 (s, 6H, H-50/51), 0.89 (s, 9H, H-53/54/55), 6.38 (dd, 1.6 and 2.4 Hz, 1H, H-2), 6.53 (dd, 1.6 and 2.4 Hz, 1H, H-42), 6.68-6.73 (m, 5H, H-15/17/22/24/40), 6.78-6.99 (m, 15H, H-
7/8/9/10/11/28/29/30/31/32/35/36/37/38/39), 7.01-7.05 (m, 4H, H-14/18/21/25), 7.31-7.33 (m, 3H, H-47/48/49) and 7.43-7.46 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: -4.5 (C-50/51), 18.2 (C-52), 25.8 (C-53/54/55), 88.4 (C-44), 89.6 (C-43), [(119.9, 120.8, 122.6, 123.5, 125.7, 126.0, 127.0, 127.2, 127.2, 128.2, 128.4, 130.2, 130.2, 131.1, 131.3, 131.3, 131.6, 133.0), Ar-CH], [(139.0, 139.2, 139.4, 139.4, 139.8, 139.9, 140.1, 140.4, 140.6, 140.9, 141.9), quarternary Ar-C] and 154.3 (C-1); FTIR (neat) $\nu_{max}$ (cm$^{-1}$): [3080, 3056, 3026 (w, Ar C–H stretch)], [2953, 2927, 2884, 2855 (w, $sp^3$ C–H stretch)], [1579, 1491 (m, Ar C=C stretch)], [1402 (m, Si–C stretch)], 1386 (m, $sp^3$ C–H bend), 1245 (m, Si–O stretch), 1195 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{max}$ (nm): 249, 286 and 304 (log $\varepsilon$ 4.87, 4.67 and 4.43); Fluorescence (CH$_2$Cl$_2$, $\lambda_{exc}$ 376 nm) $\lambda_{ems}$ (nm): 413, 438 and 464; HRMS Calcd for C$_{56}$H$_{46}$Br$_2$OSi [M]+ (monoisotopic): 921.1763, Found: 921.1780.

Monoadduct MonoHexa-H-(4-Fluorophenyl)-Br (180)

Compounds 142 (0.2830 g, 0.52 mmol, 1.0 equiv.), 132 (0.2500 g, 0.80 mmol, 1.5 equiv.) and anhydrous o-xylene (3 mL) were treated as described in General Procedure E at 200 °C for 18 d. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 99.5:0.5) followed by preparative TLC (SiO$_2$, hexane/Et$_2$O = 99:1) afforded 180 (0.1188 g, 27%) as a yellow powder. TLC $R_f$ = 0.16 (hexane/EtOAc = 97.5:2.5) and 0.08 (hexane/Et$_2$O = 98:2); melting point = 221-222 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 6.55-6.63 (m, 2H), 6.67-6.70 (m, 4H), 6.74-6.95 (m, 14H), 6.98-7.04 (m, 8H) and 7.38-7.43 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 87.8 (C-43), 89.2 (d, $^2J_{C-F}$ = 1.5 Hz, C-44), [(114.0 (d, $^2J_{C-F}$ = 21.1 Hz), 114.1 (d, $^2J_{C-F}$ = 21.1 Hz), 115.6, 115.8, 119.5, 119.5, 120.0, 121.8, 125.9, 126.0, 127.1, 127.1, 127.2, 127.2, 129.0, 130.2, 131.1, 131.2, 131.2, 131.3, 132.7 (d, $^3J_{C-F}$ = 7.9 Hz), 132.8 (d, $^3J_{C-F}$ = 8.1 Hz), 132.9, 133.5, 133.5, 134.3), Ar-CH], [(136.0 (d, $^4J_{C-F}$ = 3.6 Hz), 139.2, 139.2, 139.3, 139.3, 139.7, 139.9, 139.9, 140.2, 140.5, 140.6, 140.8), quarternary Ar-C], [(160.9 (d, $^1J_{C-F}$ = 243.8 Hz), 162.5 (d, $^1J_{C-F}$ = 247.7 Hz), C–F]); $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ ppm: -116.58 and -111.09; FTIR (neat) $\nu_{max}$ (cm$^{-1}$): [3080, 3056, 3026 (w, Ar C–H stretch)], [1595 (m), 1507 (s) (Ar C=C stretch)], 1220 (s, Ar C–F stretch) and 1071 (s, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{max}$ (nm): 250, 282 and 302 (log $\varepsilon$ 4.83, 4.69
and 4.43); **Fluorescence** (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{em}}$ (nm): 413, 437 and 463; **ASAP-MS** [M]$^+$ $m/z$ = 826 (48%), 827 (24%), 828 (100%), 829 (72%), 830 (41%), 831 (22%) and 832 (6%); **HRMS** Calcd for C$_{50}$H$_{30}$Br$_2$F$_2$ [M]$^+$ (monoisotopic): 826.0677, Found: 826.0673.

**Monoadduct MonoHexa-OH-(4-Fluorophenyl)-Br (181)**

Compounds 142 (0.5020 g, 0.9 mmol, 1.0 equiv.), 133 (0.4595 g, 1.4 mmol, 1.5 equiv.) and anhydrous o-xylene (5 mL) were treated as described in General Procedure E at 200 °C for 5 d. Purification by reverse-phase HPLC (ACN/H$_2$O = 90:10 to 100:0) afforded 181 (0.3901 g, 50%) as a light brown-to-yellow powder and diadduct 170 (0.1744 g, 28%) as a pale yellow powder.

**TLC** $R_f$ = 0.20 (hexane/Et$_2$O = 2:1); **melting point** = 176-177 °C; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ ppm: 4.57 ($s$, 1H, OH), 6.29 ($dd$, 1.4 and 2.5 Hz, 1H), 6.49 ($dd$, 1.4 and 2.5 Hz, 1H), 6.58-6.70 ($m$, 7H), 6.75-6.86 ($m$, 6H), 6.88-7.04 ($m$, 12H) and 7.37-7.42 ($m$, 2H); **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ ppm: 87.8 (C-43), 88.8 ($d$, $^2$J$_{C,F}$ = 1.4 Hz), [(114.0 ($d$, $^2$J$_{C,F}$ = 21.2 Hz), 114.1 ($d$, $^2$J$_{C,F}$ = 21.1 Hz), 115.6, 115.7, 115.8, 118.9, 119.3, 119.4, 120.0, 122.8, 125.9, 126.1, 127.2, 127.2, 127.3, 127.6, 130.2, 131.0, 131.1, 131.2, 131.2, 132.5 ($d$, $^3$J$_{C,F}$ = 7.9 Hz), 132.7 ($d$, $^3$J$_{C,F}$ = 7.8 Hz), 132.91, 133.50, 133.58), Ar-CH], [(135.9 ($d$, $^4$J$_{C,F}$ = 3.5 Hz), 139.2, 139.2, 139.3, 139.4, 139.6, 139.7, 139.8, 139.8, 140.5, 140.8, 142.2), quarternary Ar-C], 154.12 (C-1), [(160.9 ($d$, $^4$J$_{C,F}$ = 243.8 Hz), 162.6 ($d$, $^4$J$_{C,F}$ = 248.1 Hz), C–F]; **$^{19}$F NMR** (470 MHz, CDCl$_3$) $\delta$ ppm: -116.44 and -110.90; **FTIR** (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3554 (w, O–H stretch), [3052, 3025 (w, Ar C–H stretch)], [1586, 1508, 1493 (m, Ar C=C stretch)], 1221 (m, Ar C–F stretch), 1177 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); **UV/Vis** (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 250, 284 and 305 (log $\varepsilon$ 4.86, 4.67 and 4.35); **Fluorescence** (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{em}}$ (nm): 413, 437 and 464; **ASAP-MS** [M+H]$^+$ $m/z$ = 843 (45%), 844 (22%), 845 (100%), 846 (47%), 847 (40%), 848 (16%) and 849 (3%); **HRMS** Calcd for C$_{50}$H$_{31}$Br$_2$F$_2$O [M+H]$^+$ (monoisotopic): 843.0704, Found: 843.0699.

**Monoadduct MonoHexa-H-(2-Fluorophenyl)-Br (182)**

Compounds 142 (0.2774 g, 0.52 mmol, 1.0 equiv.), 134 (0.2411 g, 0.77 mmol, 1.5
equiv.) and anhydrous o-xylene (3 mL) were treated as described in General Procedure E at 200 °C for 7 d. Purification by flash column chromatography (SiO₂, petroleum ether/EtOAc = 95:5) followed by preparative TLC (SiO₂, hexane/EtOAc = 97:3) afforded 182 (0.2521 g, 60%) as a yellow powder. The diadduct by-product 171 (0.1213 g, 17%) was also isolated as a pale yellow powder.

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TLC \text{ RF} = 0.13 \text{ (hexane/EtOAc = 97.5:2.5); melting point} = 141-142 ^\circ C; \text{ }^1H NMR (400 MHz, CDCl}_3 \delta \text{ ppm: } 6.58-6.76 (m, 6H), 6.80-6.97 (m, 14H), 7.03-7.31 (m, 1H), and 7.40-7.45 (m, 1H); \text{ }^{13}C NMR (100 MHz, CDCl}_3 \delta \text{ ppm: [82.1 (d, }^3J_{C-F} = 12.0 \text{ Hz), 94.6 (d, }^3J_{C-F} = 3.4 \text{ Hz), 94.7 (d, }^3J_{C-F} = 3.5 \text{ Hz)), C=C], [(112.1, 114.4, 114.6, 114.7, 114.8, 115.5, 115.7, 120.0, 121.2, 121.7, 122.8, 122.9, 123.0, 123.1, 124.0, 124.0, 124.0, 124.0, 124.0, 126.1, 126.7, 126.8, 126.9, 127.1, 127.2, 127.2, 127.3, 127.3, 128.1, 128.1, 128.2, 128.3, 128.7, 128.8, 129.3, 129.9, 129.9, 129.9, 130.2, 130.2, 130.3, 130.3, 130.4, 130.5, 130.7, 130.8, 130.8, 131.0, 131.1, 131.2, 131.3, 131.4, 132.5, 132.5, 132.8, 132.8, 132.9, 132.9, 132.9, 133.0, 133.0, 133.5, 133.5, 133.8, 134.1, 135.1, 135.2), Ar-CH], [(139.1, 139.2, 139.6, 139.7, 139.7, 140.3, 140.5, 140.5, 140.7, 141.3, 141.3), quarternary Ar-C], [(159.4 (d, }^1J_{C-F} = 242.0 \text{ Hz), 159.5 (d, }^1J_{C-F} = 242.3 \text{ Hz), 162.7 (d, }^1J_{C-F} = 249.3 \text{ Hz), 162.7 (d, }^1J_{C-F} = 250.9 \text{ Hz)), C–F]; \text{ }^{19}F NMR (470 MHz, CDCl}_3 \delta \text{ ppm: } -112.03, -111.50, -110.04 \text{ and } -109.95; \text{ FTIR (neat)} \nu_{max} (\text{cm}^{-1}): [3056, 3027 \text{ (w, Ar C–H stretch)}], [1598, 1574, 1492 \text{ (m, Ar C=C stretch)}], 1225 \text{ (m, Ar C–F stretch) and 1072} \text{ (m, Ar C–Br stretch); UV/Vis (CH}_2Cl}_2 \lambda_{max} (\text{nm}): 248, 283 \text{ and 304 (log } \varepsilon 4.78, 4.67 \text{ and 4.48); Fluorescence (CH}_2Cl}_2, \lambda_{exc} 376 \text{ nm) } \lambda_{ems} (\text{nm}): 413, 437 \text{ and 464; ASAP-MS } [\text{M+NH}_4]^+ m/z = 844 (49%), 845 (28%), 846 (100%), 847 (53%), 848 (41%), 849 (25%) \text{ and } 850 (4%); \text{ HRMS Calcd for } \text{C}_{50}\text{H}_{34}\text{N}_{79}\text{Br}_{2}\text{F}_2 [\text{M+NH}_4]^+ (\text{monoisotopic): 844.1021, Found: 844.1032.}

Monoadduct MonoHexa-OH-(2-Fluorophenyl)-Br (183)

Compounds 142 (0.5576 g, 1.0 mmol, 1.0 equiv.), 135 (0.5032 g, 1.5 mmol, 1.5 equiv.) and anhydrous o-xylene (5 mL) were treated as described in General Procedure E at 200 °C for 5 d. Purification by reverse-phase HPLC (ACN/H₂O = 90:10 to 100:0) afforded 183 (0.3498 g, 40%) and diadduct 173 (0.1419 g, 20%) both obtained as pale yellow powders.
Experimental

TLC $R_f$ of 183 = 0.13 (hexane/EtOAc = 4:1); melting point = 158-159 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 4.79 (s, 1H, OH), 4.81 (s, 1H, OH), 6.33 (dd, 1.4 and 2.4 Hz, 1H), 6.44 (dd, 1.4 and 2.4 Hz, 1H), 6.51-6.53 (m, 2H), 6.60-6.98 (m, 3H), 7.02-7.10 (m, 12H), 7.25-7.31 (m, 2H) and 7.38-7.43 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(82.1 (d, $^3$J$_{C-F}$ = 12.9 Hz), 94.2 (d, $^4$J$_{C-F}$ = 3.0 Hz), C≡C], [(111.9, 111.9, 112.1, 114.4, 114.6, 114.6, 115.5, 115.7, 116.0, 118.3, 118.7, 120.0, 122.3, 122.6, 122.9, 122.9, 123.1, 123.1, 124.0, 124.0, 126.1, 126.1, 126.7, 126.8, 126.9, 127.1, 127.2, 127.3, 127.3, 127.4, 127.9, 127.9, 128.1, 128.1, 128.8, 128.9, 128.9, 130.0, 130.1, 130.1, 130.2, 130.2, 130.3, 130.3, 130.4, 130.7, 130.7, 131.0, 131.0, 131.1, 131.2, 132.4 (d, $^3$J$_{C-F}$ = 24.5 Hz), 132.5 (d, $^3$J$_{C-F}$ = 24.4 Hz), 132.8, 132.9, 132.9, 132.9, 133.0, 133.5, 133.5), Ar-CH], [(134.9, 135.0, 139.1, 139.1, 139.3, 139.5, 139.5, 139.6, 139.6, 139.6, 140.2, 140.2, 140.4, 141.3, 141.3, 141.8, 141.8), quarternary Ar-C], [(153.9, 154.2), C–O], [(159.4 (d, $^1$J$_{C-F}$ = 241.8 Hz), 159.5 (d, $^1$J$_{C-F}$ = 242.3 Hz), 162.7 (d, $^1$J$_{C-F}$ = 249.5 Hz), 162.7 (d, $^1$J$_{C-F}$ = 249.7 Hz), C–F]; $^{19}$F NMR (470 MHz, CDCl$_3$) δ ppm: -112.00, -111.50, -109.96 and -109.88; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3547 (w, O–H stretch), [3056, 3025 (w, Ar C–H stretch)], [1586, 1492 (m, Ar C–H stretch)], [1215 (m, Ar C–F stretch), 1175 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 246, 278 and 307 (log $\varepsilon$ 4.89, 4.68 and 4.41); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 412, 437 and 463; ASAP-MS [M]$^+$ and [M+H]$^+$ $m/z$ = 842 (7%), 843 (35%), 844 (28%), 845 (100%), 846 (53%), 847 (47%), 848 (17%) and 849 (2%); HRMS Calcd for C$_{50}$H$_{30}$F$_2$O [M]$^+$ (monoisotopic): 842.0626, Found: 842.0624 and Calcd for C$_{50}$H$_{31}$F$_2$O [M+H]$^+$ (monoisotopic): 843.0704, Found: 843.0702.

6.6.3 Synthesis of Unsymmetrical Hexaaryl Dendrimers

Dendrimer Hexa-H-Phenyl-Br-F (184)

Compounds 178 (28.1 mg, 0.036 mmol, 1.0 equiv.) and 143 (14.8 mg, 0.036 mmol, 1.0 equiv.) and anhydrous o-xylene (1 mL) were treated as described in General Procedure E at 200 °C for 3 d. Purification by preparative TLC (SiO$_2$, hexane/EtOAc = 97.5:2.5) afforded 184 (25.7 mg, 61%) as a pale yellow powder.
Experimental

TLC \( R_f = 0.10 \) (hexane/EtOAc \( = 97.5:2.5 \)); melting point \( > 300 \) °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 6.07-6.15 (m, 4H), 6.23-6.27 (m, 3H), 6.51-6.58 (m, 6H), 6.60-6.73 (m, 11H), 6.77-6.87 (m, 14H) and 6.91-7.03 (m, 12); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: [(113.7 (d, \( ^{2}J_{C-F} = 21.1 \) Hz), 113.8 (d, \( ^{2}J_{C-F} = 21.1 \) Hz)), Ar-CH], [(119.6, 119.7), C–Br], [(125.2, 125.3, 125.4, 125.4, 125.5, 125.6, 126.7, 126.8, 126.9, 127.0, 127.1, 127.2, 127.3, 129.0, 129.1, 129.9, 130.1, 131.3, 131.3, 131.4, 134.4, 134.5, 131.7, 131.8, 132.7, 132.7, 132.8, 132.8, 132.8, 132.9, 133.0, 133.1, 135.7), Ar-CH], [136.6 (d, \( ^{4}J_{C-F} = 3.6 \) Hz), 136.7 (d, \( ^{4}J_{C-F} = 3.1 \) Hz), 138.7, 138.8, 139.2, 139.2, 139.4, 139.5, 139.7, 139.7, 140.3, 140.3, 140.4, 140.4, 140.5, 140.5, 140.5, 140.5, 140.6, 140.7, 140.9) quarternary Ar-C], [(160.6 (d, \( ^{1}J_{C-F} = 243.6 \) Hz), 160.7 (d, \( ^{1}J_{C-F} = 243.1 \) Hz), C–F]; \(^1\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) ppm: -117.23, -117.21 and -117.12; FTIR (neat) \( \nu_{max} \) (cm\(^{-1}\)): [3054, 3026 (w, Ar C–H stretch)], [1601, 1510, 1493 (m, Ar C=C stretch)], 1223 (m, Ar C–C stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \( \lambda_{max} \) (nm): 251 and 281 (log \( \varepsilon \) 4.99 and 4.59); Fluorescence (CH\(_2\)Cl\(_2\), \( \lambda_{exc} \) 376 nm) \( \lambda_{ems} \) (nm): 412, 436 and 465; MALDI-TOF-MS (DCTB) Calcd for C\(_{78}\)H\(_{50}\)Br\(_2\)F\(_2\) [M]\(^{+}\): 1184.2 (100%), Found: 1184.2 (100%).

Dendrimer Hexa-OTBDMS-Phenyl-Br-F (185)

Compounds 179 (0.1048 g, 0.11 mmol, 1.0 equiv.), 143 (0.0749 g, 0.18 mmol, 1.6 equiv.) and anhydrous o-xylene (1 mL) were treated as described in General Procedure E at 200 °C for 4 d. Purification by preparative TLC (SiO\(_2\), hexane/Et\(_2\)O = 97:3) and precipitation in acetonitrile gave 185 (0.1089 g, 73%) as a pale yellow powder.

TLC \( R_f = 0.13 \) (hexane/EtO\(_2\)O = 97:3); melting point \( = 267-268 \) °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: -0.31 (s, 6H, H-79/80), 0.69 (s, 9H, H-82/83/84), 5.79 (\( dd \), 1.5 and 2.3 Hz, 1H, H-2), 5.80 (\( dd \), 1.5 and 2.3 Hz, 1H, H-42), 6.11-6.18 (m, 4H), 6.25 (t, 1.2 Hz, \(^1\)H, H-40), 6.50-6.56 (m, 6H), 6.59-6.73 (m, 10H) and 6.76-7.02 (m, 26H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \)
Experimental

ppm: -4.6 (C-79/80), 18.0 (C-82/83/84), [(113.7 (d, $^2J_{CF} = 21.1$ Hz), 113.8 (d, $^2J_{CF} = 20.8$ Hz), Ar-CH), [(119.6, 119.7), C-Br], [(121.3, 121.5, 125.3, 125.4, 125.5, 125.5, 125.7, 126.6, 126.7, 126.8, 126.9, 127.0, 127.2, 127.3, 127.4, 129.1 (C-40), 129.9, 130.0, 130.1, 131.2, 131.1, 131.3, 131.6, 131.7, 132.7, 132.8, 132.9, 133.0, 133.0), Ar-CH], [(113.7 (d, $^4J_{CF} = 3.7$ Hz), 136.8 (d, $^4J_{CF} = 3.2$ Hz)], 138.6, 139.1, 139.1, 139.4, 139.6, 139.6, 139.7, 139.7, 139.8, 140.3, 140.3, 140.4, 140.4, 140.5, 140.5, 140.6, 140.7, 140.7, 140.8, 140.8), quarternary Ar-C], 153.2 (C-1), [(160.6 (d, $^1J_{CF} = 243.0$ Hz), 160.7 (d, $^1J_{CF} = 243.0$ Hz), C-F); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -117.28, -117.26 and -117.16; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3055, 3026 (w, Ar C–H stretch)], [2954, 2926, 2854 (w, sp$^3$ C–H stretch), [1587, 1511, 1493 (m Ar C=C stretch)], 1389 (m, sp$^3$ C–H bend), 1263 (m, Si–O stretch), 1224 (m, Ar C–F stretch), 1194 (m, C–O stretch) and 1073 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 251, 278 and 300 (log $\varepsilon$ 5.05, 4.70 and 4.07); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 412, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C$_{84}$H$_{64}$Br$_2$F$_2$OSi [M]$^+$: 1314.3 (100%), Found: 1314.3 (100%).

Dendrimer Hexa-OH-Phenyl-Br-F (186)

Compounds 185 (0.1089 g, 0.08 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 0.1 mL, 0.1 mmol, 1.2 equiv.) and anhydrous THF (2 mL) were treated as described in General Procedure B. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 9:1 to 4:1) afforded 186 (0.0825 g, 83%) as a white powder.

TLC $R_f$ = 0.23 (hexane/EtOAc = 4:1); melting point = 210 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 5.74 (dd, 1.4 and 2.4 Hz, 1H, H-2), 5.75 (dd, 1.4 and 2.4 Hz, 1H, H-42), 6.10-6.16 (m, 4H), 6.25 (t, 1.4 Hz, 1H, H-40), 6.50-6.74 (m, 16H) and 6.79-7.04 (m, 26H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: [(113.7 (d, $^2J_{CF} = 21.2$ Hz), 113.8 (d, $^2J_{CF} = 21.1$ Hz), 116.3, 116.4, Ar-CH), [(119.7, 119.8), C–Br], [(125.3, 125.5, 125.6, 125.7, 126.7, 126.8, 126.8, 126.9, 127.0, 127.2, 127.3, 127.4, 129.0 (C-40), 129.9, 130.0, 131.2, 131.2, 131.3, 131.3, 131.6, 132.7, 132.7, 132.8, 132.9, 133.0, 133.0), Ar-CH], [(136.6 (d, $^4J_{CF} = 3.2$ Hz), 136.7 (d, $^4J_{CF} = 3.2$ Hz), 138.8, 138.9, 139.2, 139.2, 139.3, 139.5, 139.6, 139.7, 140.1, 140.2, 140.2, 140.2, 140.3, 140.3, 140.4, 140.5, 140.5, 140.7, 140.9), quarternary Ar-C], 153.1 (C-1), [(160.6 (d, 264
**Experimental**

$^{1}J_{C-F} = 243.4$ Hz), 160.7 ($d$, $^{1}J_{C-F} = 243.7$ Hz)), C–F; $^{19}F$ NMR (376 MHz, CDCl$_3$) δ ppm: -117.17, -117.16 and -117.07; FTIR (neat) $v_{\text{max}}$ (cm$^{-1}$): 3564 (w, O–H stretch), [3054, 3025 (w, Ar C–H stretch)], [1592, 1510, 1492 (m, Ar C=C stretch)], 1222 (m, Ar C–F stretch), 1188 (w, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 250, 278 and 300 (log $\varepsilon$ 5.06, 4.66 and 4.08); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 436 and 462; MALDI-TOF-MS (DCTB) Calcd for C$_{78}$H$_{50}$Br$_2$F$_2$O [M]$^{+}$: 1200 (100%), Found: 1200 (100%).

**Dendrimer Hexa-H-(4-Fluorophenyl)-Br-F (187)**

Compounds 180 (0.0536 g, 0.07 mmol, 1.0 equiv.), 143 (0.0816 g, 0.19 mmol, 3.0 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 4 d. Purification by preparative TLC (SiO$_2$, hexane/EtOAc = 95:5) afforded 187 (0.0548 g, 69%) as a pale yellow powder.

TLC $R_f$ = 0.14 (hexane/EtOAc = 20:1); melting point = > 300 °C; $^{1}H$ NMR (400 MHz, CDCl$_3$) δ ppm: 5.63-5.69 (m, 2H), 6.08-6.16 (m, 4H), 6.25-6.33 (m, 6H), 6.44 (td, 2.7 and 8.8 Hz, 2H), 6.49-6.80 (m, 48H), 6.84-6.87 (m, 16H), 6.94-7.06 (m, 16H) and 7.09-7.13 (m, 2H); $^{13}C$ NMR (100 MHz, CDCl$_3$) δ ppm: [(113.5, 113.6, 113.7, 113.8, 113.9 ($d$, $^{2}J_{C-F} = 21.3$ Hz), 113.9, 114.2, 114.2, 119.7, 119.8, 125.5, 125.6, 125.6, 125.7, 125.7, 125.8, 125.9, 126.9, 127.0, 127.0, 127.1, 127.1, 127.1, 127.2, 127.2, 127.3, 127.4, 129.1, 129.1, 129.2, 129.2, 130.0, 130.0, 130.1, 131.1, 131.2, 131.2, 131.3, 131.3, 131.6, 131.7, 131.7, 132.5, 132.6, 132.7, 132.8, 132.9, 132.9, 133.0, 133.2, 133.2, 133.3, 135.5), Ar-CH], [(136.2 ($d$, $^{4}J_{C-F} = 3.1$ Hz), 136.3 ($d$, $^{4}J_{C-F} = 3.6$ Hz), 136.4, 136.5, 136.5, 136.5, 136.6, 136.6, 136.6, 136.6, 136.7, 138.7, 138.7, 138.7, 138.8, 138.9, 139.3, 139.4, 139.4, 139.4, 139.5, 139.5, 139.6, 139.6, 139.7, 139.8, 139.9, 140.0, 140.1, 140.2, 140.3, 140.4, 140.4, 140.5, 140.5, 140.6, 140.6, 140.7, 140.8, 140.9, 141.0, 141.1), quarternary Ar-C], [(160.6 ($d$, $^{1}J_{C-F} = 242.9$ Hz), 160.6 ($d$, $^{1}J_{C-F} = 243.3$ Hz), 160.7 ($d$, $^{1}J_{C-F} = 243.7$ Hz), 160.8 ($d$, $^{1}J_{C-F} = 243.1$ Hz), 160.8 ($d$, $^{1}J_{C-F} = 243.2$ Hz)), C–F]; $^{19}F$ NMR (470 MHz, CDCl$_3$) δ ppm: -117.14, -117.06, -117.03, -117.02, -116.91, -116.91, -116.79 and -116.68; FTIR (neat) $v_{\text{max}}$ (cm$^{-1}$): [3052, 3026 (w, Ar C–H stretch)], [1602 (m), 1510 (s) (Ar C=C stretch)], 1221 (m, Ar C–F stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 250 and 278 (log $\varepsilon$ 5.09 and 4.72); Fluorescence
Experimental

(CH₂Cl₂, λ<sub>exc</sub> 376 nm) λ<sub>ems</sub> (nm): 412, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C₇₈H₄₈Br₂F₄ [M]+: 1220.2 (100%), Found: 1220.2 (100%).

Dendrimer Hexa-OH-(4-Fluorophenyl)-Br-F (188)

Compounds 181 (0.1029 g, 0.12 mmol, 1.0 equiv.), 143 (0.0780 g, 0.18 mmol, 1.5 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure 200 °C for 14 d. Purification by reverse-phase HPLC (ACN/H₂O = 90:10 to 100:0) afforded to give yellow powder of 188 (0.0961 g, 64%).

TLC R<sub>f</sub> = 0.38 (hexane/Et₂O = 3:2); melting point = 189-190 °C (decomposition); <sup>1</sup>H NMR (400 MHz, CDCl₃) δ ppm: 3.92 (s, 2H, OH), 5.70-5.80 (m, 6H), 6.09-6.17 (m, 4H), 6.19 (t, 1.4 Hz, 1H), 6.21 (t, 1.4 Hz, 1H), 6.45-6.89 (m, 64H), 6.94-7.07 (m, 16H) and 7.10-7.14 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl₃) δ ppm: [(113.6, 113.6, 113.6, 113.7, 113.8, 113.8, 113.8, 113.8, 114.0, 114.1, 114.1, 114.3, 114.3, 114.4, 116.4, 116.4, 116.5, 116.5, 119.8, 119.9, 125.5, 125.7, 125.8, 125.9, 126.0, 126.9, 127.0, 127.0, 127.1, 127.1, 127.1, 127.2, 127.2, 127.2, 127.2, 127.3, 127.4, 127.5, 128.8, 128.8, 130.0, 130.0, 130.1, 131.1, 131.2, 131.3, 131.3, 131.5, 131.6, 132.5, 132.5, 132.5, 132.6, 132.6, 132.7, 132.8, 132.8, 132.9, 133.0, 133.0, 133.0, 133.0, 133.1, 133.1, 133.1, 133.1], Ar-CH], [(136.1, 136.1, 136.2, 136.2, 136.3, 136.4, 136.4, 136.5, 138.9, 139.0, 139.2, 139.3, 139.4, 139.4, 139.5, 139.5, 139.6, 139.6, 139.7, 140.0, 140.0, 140.1, 140.2, 140.3, 140.3, 140.4, 140.4, 140.5, 140.6, 140.6, 140.8, 141.0, 141.0, 141.1), quarternary Ar-C], [(153.3, 153.3), C–O], [(159.5, 159.5, 159.5, 159.6, 159.6, 161.9, 161.9, 162.0), C–F]; <sup>19</sup>F NMR (470 MHz, CDCl₃) δ ppm: -117.02, -117.00, -116.90, -116.90, -116.82, -116.62 and -116.51; FTIR (neat) ν<sub>max</sub> (cm<sup>-1</sup>): 3572 (w, O–H stretch), [3053, 3026 (w, Ar C–H stretch)], [1593, 1510 (m, Ar C=C stretch)], 1220 (m, Ar C–F stretch), 1157 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH₂Cl₂) λ<sub>max</sub> (nm): 250, 277 and 300 (log ε 5.08, 4.71 and 4.10); Fluorescence (CH₂Cl₂, λ<sub>exc</sub> 376 nm) λ<sub>ems</sub> (nm): 413, 437 and 464; MALDI-TOF-MS (DCTB) Calcd for C₇₈H₄₈Br₂F₄O [M]+: 1236.2 (100%), Found: 1236.2 (100%).

Dendrimer Hexa-H-(2-Fluorophenyl)-Br-F (189)

Compounds 182 (0.0951 g, 0.11 mmol, 1.0 equiv.), 143 (0.0749 g, 0.18 mmol, 1.6
equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 22 d. Purification by reverse-phase HPLC (ACN 100%) afforded 189 (0.1016 g, 73%) as a yellow powder.

**TLC** $R_f = 0.10$ (hexane/EtOAc = 20:1);

**$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ ppm: 5.32-5.35 (m, 2H), 5.38-5.52 (m, 8H), 6.01-6.07 (m, 3H), 6.11-7.15 (m, 36H) and 7.18-7.22 (m, 3H);

**$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ ppm: [(113.6, 113.8, 113.9, 114.0, 114.1, 114.3, 114.4, 114.6, 114.7, 114.8, 114.9, 119.8, 119.9, 122.9, 123.1, 123.2, 123.2, 125.1, 125.2, 125.3, 125.4, 125.4, 125.5, 125.6, 125.6, 125.7, 125.8, 125.8, 125.9, 126.1, 126.1, 126.2, 126.2, 126.3, 126.5, 126.6, 126.6, 126.7, 126.7, 126.9, 126.9, 127.0, 127.1, 127.1, 127.1, 127.2, 127.3, 127.3, 127.4, 127.4, 127.5, 127.9, 127.9, 128.1, 128.3, 128.3, 128.4, 128.4, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 128.9, 128.9, 129.0, 129.0, 129.1, 129.1, 129.2, 129.3, 129.3, 129.5, 129.6, 129.9, 129.9, 130.0, 130.0, 130.1, 130.1, 130.3, 130.5, 130.5, 130.6, 130.7, 130.7, 130.8, 130.9, 130.9, 131.2, 131.2, 131.2, 131.4, 131.6, 131.7, 131.8, 131.8, 131.8, 131.9, 132.0, 132.1, 132.2, 132.2, 132.2, 132.3, 132.5, 132.6, 132.7, 132.7, 132.7, 132.8, 132.8, 132.9, 133.0, 133.1, 133.1, 133.1, 133.1, 133.1, 133.5, 133.5, 133.6, 134.0, 134.2, 134.3, 134.3, 134.4, 134.5, 134.5, 134.6, 134.6, 134.7, 134.7), Ar-CH], [(136.3, 136.4, 136.6, 136.6, 136.6, 136.6, 136.6, 136.7, 138.0, 138.1, 138.2, 138.3, 138.4, 138.4, 138.6, 138.6, 138.6, 138.7, 138.7, 138.7, 138.7, 138.8, 138.8, 138.9, 139.0, 139.0, 139.2, 139.3, 139.3, 139.4, 139.5, 139.5, 139.5, 139.6, 139.6, 139.7, 139.7, 139.7, 139.8, 139.8, 139.9, 139.9, 139.9, 140.0, 140.0, 140.1, 140.1, 140.2, 140.2, 140.3, 140.3, 140.3, 140.4, 140.4, 140.4, 140.5, 140.5, 140.5, 140.6, 140.6, 140.7, 140.7, 140.8, 140.8, 140.8, 140.9, 140.9, 141.4, 141.5, 141.5, 141.5, 141.6, 141.6, 141.7, 141.7, 141.8), quarternary Ar-C], [(158.4, 158.4, 158.5, 158.5, 158.5, 158.5, 158.6, 158.6, 158.6, 159.4, 159.5, 160.8, 160.9, 160.9, 160.9, 161.0, 161.0, 161.2, 161.2, 161.2, 161.9, 161.9), C–F]; **$^{19}$F NMR** (470 MHz, CDCl$_3$) $\delta$ ppm: -117.14, -117.09, -117.05, -117.03, -117.02, -117.00, -116.98, -116.97, -116.95, -116.93, -116.93, -116.92, -115.64, -112.18, -112.16, -112.15, -111.87, -111.84, -111.11, -111.10, -110.90, -110.88, -110.63, -110.61 and -110.53 (ABq. $\Delta\delta_{AB} = 6.67$ Hz, $J_{AB} = \frac{TS}{J_{F-F}} = 3.7$ Hz); **FTIR** (neat) $\nu_{max}$ (cm$^{-1}$): [3055, 3027 (w, Ar C–H stretch)], [1602, 1580, 1510, 1491 (m, Ar C–C]
Experimental 

stretch)], 1227 (m, Ar C–F stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH₂Cl₂) λ_max (nm): 249 and 279 (log ε 5.14 and 4.65); Fluorescence (CH₂Cl₂, λ exc 376 nm) λ ems (nm): 413, 436 and 463; MALDI-TOF-MS (DCTB) Calcd for C₇₈H₄₈Br₂F₄ [M]+: 1220.2 (100%), Found: 1220.2 (100%).

Dendrimer Hexa-OH-(2-Fluorophenyl)-Br-F (190)

Compounds 183 (0.1100 g, 0.13 mmol, 1.0 equiv.), 143 (0.0860 g, 0.20 mmol, 1.5 equiv.) and anhydrous o-xylene (2 mL) were treated as described in General Procedure E at 200 °C for 14 d. Purification by reverse-phase HPLC (ACN/H₂O = 90:10 to 100:0) afforded 190 (0.1404 g, 87%) as a pale yellow powder.

TLC R_f = 0.35 (hexane/Et₂O = 3:2); melting point = 188 °C (decomposition); ¹H NMR (400 MHz, CDCl₃) δ ppm: 3.92 (br s, 7H), 5.37-5.56 (m, 10H), 5.73-5.82 (m, 8H), 5.88-5.92 (m, 5H), 5.99-6.07 (m, 4H), 6.11-6.25 (m, 7H), 6.31-6.34 (m, 2H), 6.39-7.16 (m, 33H) and 7.20-7.24 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm: [(113.6, 113.7, 113.8, 113.9, 114.0, 114.0, 114.1, 114.1, 114.3, 114.5, 114.7, 114.8, 115.5, 115.6, 115.6, 115.6, 115.6, 115.6, 115.8, 115.9, 116.0, 116.0, 116.0, 116.1, 116.3, 116.3, 116.4, 116.4, 116.5, 116.6, 119.8, 119.8, 119.8, 119.9, 123.0, 123.1, 123.1, 123.2, 123.3, 123.3, 125.3, 125.3, 125.4, 125.5, 125.6, 125.7, 125.7, 125.8, 125.8, 125.8, 125.9, 126.0, 126.1, 126.2, 126.2, 126.3, 126.3, 126.5, 126.6, 126.7, 126.7, 126.8, 126.9, 127.0, 127.0, 127.0, 127.1, 127.1, 127.2, 127.2, 127.3, 127.3, 127.4, 127.4, 127.4, 127.6, 127.6, 127.8, 127.9, 128.1, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.7, 128.7, 128.8, 128.8, 128.8, 129.1, 129.8, 129.8, 130.0, 130.0, 130.1, 130.2, 130.3, 130.4, 130.5, 130.5, 130.6, 130.6, 130.6, 130.7, 130.8, 130.9, 130.9, 131.0, 131.1, 131.3, 131.6, 131.6, 131.7, 131.7, 131.8, 131.9, 132.2, 132.5, 132.6, 132.6, 132.7, 132.7, 132.8, 132.9, 133.0, 133.2, 133.3, 133.3, 134.1, 134.1, 134.2, 134.2, 134.3, 134.4, 134.5, 134.6, 134.7), Ar-CH], [(136.4, 136.3, 136.5, 136.5, 136.5, 136.6, 136.6, 136.6, 136.6, 136.7, 136.7, 138.0, 138.0, 138.4, 139.0, 139.0, 139.0, 139.2, 139.2, 139.3, 139.3, 139.3, 139.4, 139.4, 139.5, 139.5, 139.5, 139.6, 139.6, 139.6, 139.7, 139.8, 139.8, 139.8, 139.9, 139.9, 140.0, 140.1, 140.1, 140.2, 140.2, 140.2, 140.3, 140.3, 140.4, 140.5, 140.5, 140.6, 140.7, 140.7, 140.8, 141.4, 141.5, 141.5, 141.6, 141.6, 141.7, 141.9, 142.0), quarternary Ar-C], [(153.1, 153.2, 153.3, 153.3, 153.4), C–O], [(158.4, 158.5, 158.5, 158.5, 158.5, 159.4, 159.5, 160.8, 160.9, 160.9, 268
161.0, 161.9, 161.9), C–F; $^19$F NMR (470 MHz, CDCl$_3$) δ ppm: -117.10, -117.07, -117.01, -117.00, -116.98, -116.98, -116.96, -116.95, -116.94, -116.92, -116.91, -116.91, -116.90, -116.90, -116.89, -116.89, -116.88, -116.87, -116.85, -111.83, -111.81, -111.11, -111.11, -111.10, -111.10, -110.98, -110.98, -110.96, -110.95, -110.94, -110.93, -110.92, -110.91, -110.91, -110.90, -110.90, -110.89, -110.89, -110.87, -110.86, -110.85, -110.84, -110.83, -110.82, -110.81, -110.58, -110.58, -110.57 and -110.51 (ABq, Δν$_{AB}$ = 7.11 Hz, $J_{AB}$ = $J_{F-F}$ = 3.1 Hz); FTIR (neat) $\nu$$_{max}$ (cm$^{-1}$): 3564 (w, O–H stretch), [3054, 3026 (w, Ar C–H stretch)], [1592, 1510, 1492 (m, Ar C=C stretch)], 1227 (m, Ar C–F stretch), 1175 (m, C-O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda$$_{max}$ (nm): 249, 278 and 300 (log $\varepsilon$ 5.04, 4.63 and 4.06); Fluorescence (CH$_2$Cl$_2$, $\lambda$$_{exc}$ 376 nm) $\lambda$$_{ems}$ (nm): 413, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C$_{78}$H$_{48}$Br$_2$F$_4$O [M]+: 1236.2 (100%), Found: 1236.2 (100%).

6.7 Synthesis of Ester of Pentaaryl Dendrimers

Ester Penta-OAAux-Br-Br (221)

Pentaaryl dendrimer 153 (117 mg, 0.10 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (24.7 mg, 0.10 mmol, 1.0 equiv.), DCC (24.7 mg, 0.12 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 6:1) afforded 221 (132.5 mg, 95%) as a pale yellow powder.

TLC $R_f$ = 0.38 (hexane/EtOAc = 4:1); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.89 ($d$, 6.8 Hz, 3H, H-71), 1.10 ($d$, 6.8 Hz, 3H, H-70), 2.66-2.75 ($m$, 1H, H-69), 4.63 ($d$, 8.0 Hz, 1H, H-68), 6.55-6.58 ($m$, 6H, H-2/22/24/36/55/57), 6.65-6.67 ($m$, 8H, H-15/17/29/31/48/50/62/64), 6.74-6.88 ($m$, 7H, H-28/30/32/34/61/63/65), 6.99 ($d$, 7.5 Hz, 4H, H-21/25/54/58), 7.04-7.08 ($m$, 8H, H-8/10/14/18/41/43/47/51), 7.18-7.21 ($m$, 8H, H-7/9/11/33/40/42/44/66), 7.74-7.78 ($m$, 2H, H-75/76) and 7.85-7.89 ($m$, 2H, H-74/77); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 19.5 (C-71), 21.0 (C-70), 29.0 (C-69), 57.6 (C-68), 120.1 (C-23/56), 120.4 (C-16/49), 121.4 (C-2/36), 123.9 (C-74/77), 126.4 (C-30/63), 126.9 (C-9/42), 127.5 (C-28/32), 127.7 (C-61/65), 128.0 (C-7/11/40/44), 129.5 (C-34), 130.2 (C-8/10/41/43), 130.3 (C-21/25/54/58), 130.6 (C-14/18/47/51), 131.5 (C-29/31), 131.6 (C-62/64), 131.9 (C-33/66), 132.0 (C-73/78), 133.2 (C-22/24/55/57), 133.3 (C-15/17/48/50), 134.5 (C-
75/76), [(138.3, 138.8, 139.2, 139.3, 139.4, 140.0, 140.4, 141.2, 141.2, 142.3), quarternary Ar-C] 149.4 (C-1), 167.3 (C-67) and 167.8 (C-72/79); FTIR (neat) \( \nu \) max (cm\(^{-1}\)): [3080, 3055, 3025 (w, Ar C–H stretch)], [2963, 2924, 2871 (w, sp\(^3\) C–H stretch)], [1771 (m), 1716 (s) (C=O stretch)], [1588, 1488 (m, Ar C=C stretch)], 1383 (m, sp\(^3\) C–H bend), 1176 (m, C–O stretch) and 1070 (m, Ar C–Br stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \( \lambda \) max (nm): [3080, 3055, 3025 (w, Ar C–H stretch)], [2963, 2924, 2871 (w, sp\(^3\) C–H stretch)], [1771 (m), 1716 (s) (C=O stretch)], [1588, 1488 (m, Ar C=C stretch)], 1383 (m, sp\(^3\) C–H bend), 1176 (m, C–O stretch) and 1070 (m, Ar C–Br stretch); Fluorescence (CH\(_2\)Cl\(_2\), \( \lambda \) exc 376 nm) \( \lambda \) ems (nm): 413, 438 and 462; MALDI-TOF-MS (dithranol) Calcd for C\(_{79}\)H\(_{53}\)Br\(_4\)NO\(_4\)K [M+K]\(^+\): 1438 (100%), Found: 1438 (100%).

Ester Penta-OAAux-F-F (222)

Pentaaryl dendrimer 154 (92.6 mg, 0.10 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (24.7 mg, 0.10 mmol, 1.0 equiv.), DCC (24.7 mg, 0.12 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH\(_2\)Cl\(_2\) (1 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO\(_2\), hexane/Et\(_2\)O = 95:5 to 85:15) afforded 222 (83.2 mg, 72%) as a pale yellow powder. TLC \( R_f \) = 0.16 (hexane/Et\(_2\)O = 4:1); melting point = 201-202 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) ppm: 0.91 (d, 6.8 Hz, 3H, H-71), 1.12 (d, 6.8 Hz, 3H, H-70), 2.68-2.77 (m, 1H, H-69), 4.65 (d, 8.0 Hz, 1H, H-68), 6.55-6.89 (m, 28H, H-2/14/15/17/18/21/22/24/25/28/29/30/31/32/36/47/48/50/51/54/55/57/58/61/62/63/64/65), 6.91 (t, 1.6 Hz, 1H, H-34), 7.08-7.10 (m, 4H, H-8/10/41/43), 7.17-7.22 (m, 8H, H-7/11/40/44), 7.75-7.77 (m, 2H, H-75/76) and 7.87-7.89 (m, 2H, H-74/77); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) ppm: 19.4 (C-71), 20.9 (C-70), 28.9 (C-69), 57.5 (C-68), 113.9 (d, \(^2\)J\(_{C-F}\) = 21.1 Hz, H-22/24/55/57), 114.2 (d, \(^2\)J\(_{C-F}\) = 21.1 Hz, H-15/17/48/50), 121.2 (C-2/36), 123.7 (C-74/77), 126.1 (C-30/63), 126.6 (C-9/42), 127.3 (C-28/32), 127.5 (C-61/65), 127.8 (C-7/11/40/44), 129.5 (C-34), 130.1 (C-8/10/41/43), 131.4 (C-29/31), 131.5 (C-62/64), 131.6 (C-33/66), 131.8 (C-73/78), 132.9 (d, \(^3\)J\(_{C-F}\) = 8.1 Hz, H-21/25/54/58), 133.0 (d, \(^3\)J\(_{C-F}\) = 8.1 Hz, H-14/18/47/50), 134.4 (C-75/76), 135.8 (d, \(^4\)J\(_{C-F}\) = 3.5 Hz, H-13/46), 136.1 (d, \(^4\)J\(_{C-F}\) = 3.5 Hz, H-20/53), [(138.6, 139.4, 139.4, 139.7, 140.8, 141.1, 141.3, 142.3), quarternary Ar-C], 149.3 (C-1), 160.8 (d, \(^1\)J\(_{C-F}\) = 243.7 Hz, H-23/56), 161.1 (d, \(^1\)J\(_{C-F}\) = 243.7 Hz, H-16/49), 167.2 (C-67) and 167.6 (C-72/79); \(^{19}\)F NMR (376 MHz, 270
**Experimental**

CDCl$_3$ $\delta$ ppm: -116.79 and -116.48; **FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$):** [3052, 3025 (w, Ar C–H stretch)], [2966, 2926, 2873 (w, $sp^3$ C–H stretch)], [1768 (m), 1719 (s) (C=O stretch)], [1603 (m), 1511 (s) (Ar C=C stretch)], 1382 (m, $sp^3$ C–H bend), 1220 (s, Ar C–F stretch) and 1177 (m, C–O stretch); **UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm):** 250 and 278 (log $\varepsilon$ 5.05 and 4.74); **Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm):** 413, 437 and 464; **MALDI-TOF-MS** (dithranol) Calcd for C$_{79}$H$_{53}$F$_4$NO$_4$Na [M+Na]$^+$: 1178.4 (100%), Found: 1178.7 (100%).

**Ester Penta-OAAux-Br-F (223)**

Pentaaryl dendrimer **158** (112.6 mg, 0.11 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (26.5 mg, 0.11 mmol, 1.0 equiv.), DCC (26.5 mg, 0.12 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO$_2$, hexane/CH$_2$Cl$_2$ = 1:1) afford **223** (126.1 mg, 92%) as a pale yellow powder.

**TLC $R_f$** = 0.33 (hexane/CH$_2$Cl$_2$ = 1:1); **melting point** = 187-188 °C; **$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm:** 0.90 ($d$, 6.8 Hz, 3H, H-71), 1.10 ($d$, 6.8 Hz, 3H, H-70), 2.67-2.75 ($m$, 1H, H-69), 4.63 ($d$, 8.0 Hz, 1H, H-68), 6.54-6.60 ($m$, 6H, H-2/22/24/36/55/57), 6.61-6.70 ($m$, 10H, H-15/17/29/31/48/50/54/58/62/64), 6.72-6.88 ($m$, 9H, H-28/30/32/34/47/51/61/63/65), 6.98-7.02 ($m$, 2H, H-21/25), 7.05-7.09 ($m$, 6H, H-8/10/14/18/41/43), 7.16-7.22 ($m$, 8H, H-7/9/11/40/44/33/42/66), 7.74-7.78 ($m$, 2H, H-75/76) and 7.85-7.90 ($m$, 2H, H-7/9/11/40/44/33/42/66); **$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm:** 19.4 (C-71), 20.9 (C-70), 28.9 (C-69), 57.5 (C-68), 114.2 ($d$, 2$^1$J$_{CF}$ = 21.1 Hz, C-48/50), 114.9 ($d$, 2$^1$J$_{CF}$ = 21.1 Hz, C-55/57), 120.0 (C-23), 120.3 (C-16), 121.2 (C-2), 121.2 (C-36), 123.7 (C-74/77), 126.1 (C-63), 126.2 (C-30), 126.6 (C-42), 126.7 (C-9), 127.3 (C-61), 127.4 (C-28), 127.5 (C-32), 127.5 (C-65), 127.8 (C-40/44), 127.9 (C-7/11), 129.4 (C-34), 130.0 (C-8/10), 130.1 (C-41/43), 130.2 (C-21/25), 130.5 (C-14/18), 131.3 (C-29), 131.4 (C-31), 131.4 (C-62), 131.4 (C-64), 131.5 (C-66), 131.8 (C-33), 131.8 (C-73/78), 133.0 (C-22/24), 133.1 (C-15/17), 132.9 ($d$, 3$^1$J$_{CF}$ = 8.1 Hz), 133.0 ($d$, 3$^1$J$_{CF}$ = 8.1 Hz), 134.4 (C-75/76), 135.8 ($d$, 4$^1$J$_{CF}$ = 3.5 Hz), 136.1 ($d$, 4$^1$J$_{CF}$ = 3.5 Hz), [(138.1, 138.7, 138.7, 139.0, 139.1, 139.3, 139.4, 139.4, 139.7, 139.9, 140.2, 140.8, 141.0, 141.0, 141.1, 141.3, 142.1, 142.3), quarternary Ar-C], 149.3
Experimental

(C-1), 160.8 (d, $^1J_{CF} = 243.7$ Hz, C-46), 161.1 (d, $^1J_{CF} = 244.0$ Hz, C-53), 167.2 (C-67) and 167.6 (C-72/79); $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -116.77 and -116.46; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3025 (w, Ar C–H stretch)], [2962, 2929, 2853 (w, $sp^3$ C–H stretch)], [1769 (m), 1719 (s) (C=O stretch)], [1603, 1511, 1490 (m, Ar C=C stretch)], 1382 (m, $sp^3$ C–H bend), 1221 (m, Ar C–F stretch), 1177 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 279 (log $\varepsilon$ 5.08 and 4.75); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{em}}$ (nm): 412, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C$_{79}$H$_{53}$Br$_2$F$_2$NO$_4$ [M]$^+$: 1277.2 (100%), Found: 1277.1 (100%).

**Ester Penta-OCAux-Br-Br (224)**

Into a 10 mL round bottom flask, anhydrous CH$_2$Cl$_2$ (2 mL), 153 (117.0 mg, 0.1 mmol), and Et$_3$N (0.1 mL, 0.7 mmol) were added and the mixture was stirred at room temperature. (1S)-(+)-10-Camphorsulfonyl chloride (50.0 mg, 0.2 mmol) was then added into the flask and the system was sealed and purged with nitrogen. The reaction mixture was stirred under nitrogen atmosphere at room temperature and judged to be complete when all of the starting materials had been consumed. The resulting mixture was washed successively with 5% solution of NH$_4$Cl (5 mL), water (10 mL), brine (10 mL) and dried over MgSO$_4$. The solvent was then removed under vacuum and the residue was purified by flash column chromatography (SiO$_2$, hexane/EtOAc = 6:1) to afford 93 (134.5 mg, 97%) as a pale yellow powder.

**TLC** $R_f$ = 0.33 (hexane/EtOAc = 4:1); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.86 (s, 3H, H-75), 1.09 (s, 3H, H-76), 1.39-1.45 (m, 1H, H-72), 1.53-1.60 (m, 1H, H-73), 1.94 (d, $^2J_{HH} = 18.4$ Hz, 1H, H-70), 1.99-2.08 (m, 1H, H-72), 2.11 (t, 4.8 Hz, 1H, H-71), 2.36-2.46 (m, 2H, H-70/73), 2.93 (d, $^2J_{HH} = 15.2$ Hz, 1H, H-67), 3.53 (d, $^2J_{HH} = 15.2$ Hz, 1H, H-67), 6.58 (d, 8.8 Hz, 4H, H-22/24/55/57), 6.66 (d, 8.8 Hz, 4H, H-15/17/48/50), 6.69-6.71 (m, 4H, H-29/31/62/64), 6.82 (d, 1.6 Hz, 2H, H-2/36), 6.85-6.94 (m, 6H, H-28/30/32/61/63/65), 6.98 (t, 1.6 Hz, 1H, H-34), 7.00 (d, 8.8 Hz, 4H, H-21/25/54/58), 7.06-7.07 (m, 4H, H-14/18/47/51), 7.08-7.09 (m, 4H, H-8/10/41/43) and 7.18-7.22 (m, 8H, H-7/9/11/33/40/42/44/66); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 19.9 (C-76), 20.2 (C-75), 25.2 (C-73), 27.0 (C-72), 42.6 (C-70), 42.9 (C-71), 47.5 (C-74), 48.0 (C-67), 58.2 (C-76), 145.1 (C-34), 157.1 (C-67), 160.8 (d, $^1J_{CF} = 243.7$ Hz, C-46), 161.1 (d, $^1J_{CF} = 244.0$ Hz, C-53), 167.2 (C-67) and 167.6 (C-72/79); $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -116.77 and -116.46; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3025 (w, Ar C–H stretch)], [2962, 2929, 2853 (w, $sp^3$ C–H stretch)], [1769 (m), 1719 (s) (C=O stretch)], [1603, 1511, 1490 (m, Ar C=C stretch)], 1382 (m, $sp^3$ C–H bend), 1221 (m, Ar C–F stretch), 1177 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 279 (log $\varepsilon$ 5.08 and 4.75); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{em}}$ (nm): 412, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C$_{79}$H$_{53}$Br$_2$F$_2$NO$_4$ [M]$^+$: 1277.2 (100%), Found: 1277.1 (100%).
Experimental

68), 120.1 (C-23/56), 120.3 (C-16/49), 121.4 (C-2/36), 126.4 (C-30/63), 126.8 (C-9/42),
127.6 (C-28/32/61/65), 127.9 (C-7/11/40/44), 130.0 (C-8/10/41/43), 130.2 (C-
21/25/54/58), 130.4 (C-33/66), 133.0 (C-22/24/55/57), 133.1 (C-15/17/48/50), [138.4, 138.6, 138.9, 139.0,
139.3, 139.5, 140.4, 140.9, 141.2, 142.8), quarternary Ar-C], 148.1 (C-1) and 214.1 (C-
69); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3025 (w, Ar C–H stretch)], [2956, 2921, 2852 (m,
sp$^3$ C–H stretch)], 1747 (m, C=O stretch), [1601, 1575, 1488 (m, Ar C=C stretch),
1374 (m, sp$^3$ C–H bend), 1169 (m, S=O and C–O stretch) and 1072 (m, Ar C–Br
stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 254 and 280 (log $\varepsilon$ 5.07 and 4.73); Fluorescence
(CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 336 nm) $\lambda_{\text{ems}}$ (nm): 371, 390 and 411; MALDI-TOF-MS (dithranol)
Calcd for C$_{76}$H$_{56}$Br$_4$O$_4$SNa [M+Na]$^+$: 1407 (100%), Found: 1407 (100%).

Ester Penta-OCAux-F-F (225)

Into a 10 mL round bottom flask, anhydrous CH$_2$Cl$_2$ (3 mL), 154 (92.6 mg, 0.1 mmol),
and Et$_3$N (0.1 mL, 0.7 mmol) were added and the mixture was stirred at room
temperature. (1S)-(+)10-Camphorsulfonyl chloride (50.1 mg, 0.2 mmol) was then added
into the flask and the system was sealed and purged with nitrogen. The reaction mixture
was stirred under nitrogen atmosphere at room temperature and judged to be complete
when all of the starting materials had been consumed. The resulting mixture was
washed successively with 5% solution of NH$_4$Cl (5 mL), water (10 mL), brine (10 mL)
and dried over MgSO$_4$. The solvent was then removed under vacuum and the residue
was purified by flash column chromatography (SiO$_2$, hexane/EtOAc = 90:10 to 80:20)
to afford 225 (91.0 mg, 80%) as a pale yellow powder.

TLC $R_f$ = 0.06 (hexane/EtOAc = 9:1); melting point = 201-202 °C; $^1$H NMR (400 MHz,
CDCl$_3$) $\delta$ ppm: 0.88 (s, 3H, H-75), 1.11 (s, 3H, H-76), 1.40-1.46 (m, 1H, H-72) 1.56-1.63 (m,
1H, H-73), 1.96 (d, $^2J_{H-H}$ = 18.4 Hz, 1H, H-70),
2.01-2.10 (m, 1H, H-72), 2.13 (t, 4.8 Hz, 1H, H-71), 2.38-2.48 (m, 2H, H-70/73), 2.95 (d, $^2J_{H-H}$
= 15.2 Hz, 1H, H-67), 3.56 (d, $^2J_{H-H}$ = 15.2
Hz, 1H, H-67), 6.56-6.61 (m, 4H, H-22/24/55/57), 6.63-6.70 (m, 8H, H-
15/17/21/25/48/50/54/58), 6.74-6.79 (m, 8H, H-14/18/29/31/47/51/62/64), 6.86 (d, 1.6
Hz, 2H, H-2/36), 6.88-6.95 (m, 6H, H-28/32/30/61/65/63), 7.04 (t, 1.6 Hz, 1H, H-34),
7.10-7.12 (m, 4H, H-8/10/41/43), 7.17-7.21 (m, 6H, H-7/9/11/40/42/44) and 7.23 (s, 2H, H-33/66); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 19.9 (C-76), 20.1 (C-75), 25.2 (C-73), 27.0 (C-72), 42.6 (C-70), 43.0 (C-71), 47.5 (C-74), 48.0 (C-67), 58.2 (C-68), 114.0 (d, $^2$J$_{C-F}$ = 3.4 Hz, C-21), 114.3 (d, $^2$J$_{C-F}$ = 21.1 Hz, C-15/17/48/50), 121.4 (C-2/36), 126.3 (C-30/63), 126.6 (C-9/42), 127.5 (C-28/32/61/65), 127.8 (C-7/11/40/44), 130.0 (C-8/10/41/43), 130.5 (C-34), 131.5 (C-29/31/62/64), 131.5 (C-33/66), 132.8 (d, $^3$J$_{C-F}$ = 7.9 Hz, C-21/25/54/58), 132.9 (d, $^3$J$_{C-F}$ = 7.9 Hz, C-14/18/47/51), 135.7 (d, $^4$J$_{C-F}$ = 3.4 Hz, C-13/46), 136.0 (d, $^4$J$_{C-F}$ = 3.4 Hz, C-20/53), [(138.9, 139.3, 139.3, 139.4, 140.9, 141.2, 141.2, 143.0), quarternary Ar-C], 148.1 (C-1), 160.9 (d, $^1$J$_{C-F}$ = 243.8 Hz, C-23/56), 161.1 (d, $^1$J$_{C-F}$ = 243.8 Hz, C-16/49) and 214.0 (C-69); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -116.67 and -116.37; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3055, 3025 (w, Ar C–H stretch)], [2958, 2889 (w, sp$^3$ C–H stretch)], 1747 (m, C=O stretch), [1603, 1580, 1511 (m, Ar C=C stretch)], 1374 (m, sp$^3$ C–H bend), 1220 (m, Ar C–F stretch), 1169 (m, S=O stretch) and 1157 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 251 and 278 (log $\varepsilon$ 5.07 and 4.75); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 436 and 464; MALDI-TOF-MS (dithranol) Calcd for C$_{75}$H$_{54}$F$_4$O$_4$SNa [M+Na]$^+$: 1163 (100%), Found: 1163 (100%).

6.8 Synthesis of Ester of Hexaaryl Dendrimers

Ester Hexa-OAAux-Phenyl-Br-Br (226)

Hexaaryl dendrimer 163 (200.2 mg, 0.15 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (37.4 mg, 0.15 mmol, 1.0 equiv.), DCC (37.4 mg, 0.18 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (3 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO$_2$, hexane/CH$_2$Cl$_2$ = 70:30 to 1:1) afforded 226 (116.5 mg, 50%) as a pale yellow powder.

TLC $R_f$ = 0.40 (hexane/CH$_2$Cl$_2$ = 1:1); melting point = 219-220 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 0.81 (d, 6.8 Hz, 3H, H-83), 0.99 (d, 6.8 Hz, 3H, H-82), 2.55-2.67 (m, 1H, H-81), 4.36 (d, 8.8 Hz, 1H, H-80), 5.81-5.89 (m, 2H), 5.92-5.93 (m, 2H), 6.28-6.37 (m, 2H), 6.41 (t, 1.6 Hz, 1H, H-40), 6.49-7.04 (m,
Experimental

42H), 7.74-7.78 (m, 2H, H-87/88) and 7.84-7.88 (m, 2H, H-86/89); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 19.3 (C-83), 20.7 (C-82), 28.2 (C-81), 57.5 (C-80), [(119.7, 119.8), C–Br], [(122.3 (C-2/42), 123.6 (C-86/89), 125.3, 125.5, 125.6, 125.8, 126.5, 126.8, 126.9, 127.1, 127.2, 127.3, 127.5, 129.9, 130.0, 130.0, 131.1, 131.2, 131.2, 131.3, 131.5, 131.6, 131.8 (C-85/90), 132.8, 132.9, 133.0, 133.0, 133.0 (C-40), 134.3 (C-87/88)), Ar-CH], [(138.6, 138.9, 139.0, 139.1, 139.2, 139.4, 139.5, 139.6, 139.7, 139.7, 139.8, 139.8, 140.0, 140.0, 140.2, 140.2, 140.4, 140.4, 140.6, 140.7, 140.8, 140.9, 140.9), quarternary Ar-C], 148.1 (C-1), 165.8 (C-79) and 167.5 (C-84/91); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3080, 3055, 3026 (w, Ar C–H stretch)], [2963, 2925, 2873, 2852 (w, sp$^3$ C–H stretch)], [1766 (w), 1719 (m) (C=O stretch)], [1601, 1587, 1491 (m, Ar C=C stretch)], 1383 (m, sp$^3$ C–H bend), 1175 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 252 and 280 (log $\varepsilon$ 5.09 and 4.73); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 438 and 462; MALDI-TOF-MS (dithranol) Calcd for C$_{91}$H$_{61}$Br$_4$NO$_4$Na [M+Na]$^+$: 1574.1 (100%), Found: 1574.4 (100%).

Ester Hexa-OAux-Phenyl-F-F (227)

Hexaaryl dendrimer 164 (215.6 mg, 0.20 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (49.4 mg, 0.20 mmol, 1.0 equiv.), DCC (49.4 mg, 0.24 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (4 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO$_2$, hexane/CH$_2$Cl$_2$ = 70:30 to 1:1) afforded 227 (130.5 mg, 50%) as a pale yellow powder.

TLC $R_f$ = 0.26 (hexane/CH$_2$Cl$_2$ = 1:1);

melting point = 190-191 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.82 (d, 6.8 Hz, 3H, H-83), 1.00 (d, 6.8 Hz, 3H, H-82), 2.58-2.67 (m, 1H, H-81), 4.37 (d, 8.8 Hz, H-80), 5.86-5.92 (m, 2H), 5.96 (d, 1.6 Hz, 2H, H-2/42), 6.32-6.38 (m, 2H), 6.45 (t, 1.6 Hz, 1H, H-40), 6.51-6.94 (m, 40H), 7.01-7.06 (m, 2H), 7.74-7.77 (m, 2H, H-87/88) and 7.85-7.88 (m, 2H, H-86/89);

$^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 19.3 (C-83), 20.7 (C-82), 28.3 (C-81), 57.5 (C-80), [(113.7 (d, $^2$$J_{C-F}$ = 21.0 Hz), 113.8 (d, $^2$$J_{C-F}$ = 21.1 Hz), 122.3 (C-2/42), 123.6 (C-86/89), 125.3, 125.3, 125.6, 126.5, 126.6, 126.7, 126.8, 126.8, 127.0, 127.2, 127.2, 127.3,
Experimental

127.5, 131.2, 131.2, 131.3, 131.4, 131.5, 131.7, 131.8 (C-85/90), 132.6, 132.7, 132.8, 132.8, 132.9, 133.2 (C-40), 134.3 (C-87/88), Ar-CH, [(136.5 (d, \(^4J_{C-F} = 3.4\) Hz, C-13/52), 136.6 (d, \(^4J_{C-F} = 3.7\) Hz, C-20/58), 138.4, 139.5, 139.6, 139.7, 139.8, 139.9, 140.0, 140.3, 140.3, 140.4, 140.5, 140.6, 140.7, 140.8, 140.9), quarternary Ar-C], 148.1 (C-1), [(160.6 (d, \(^1J_{C-F} = 243.1\) Hz), 160.7 (d, \(^1J_{C-F} = 243.3\) Hz)), C–F] 165.8 (C-79) and 167.5 (C-84/91); \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) ppm: -117.18, -117.18 and -117.09; FTIR (neat) \(\nu_{\text{max}}\) (cm\(^{-1}\)): [3054, 3026 (w, Ar C–H stretch)], [2963, 2924 (w, sp\(^3\) C–H stretch)], [1767 (m), 1720 (s) (C=O stretch)], [1603, 1510 (m, Ar C=C stretch)], 1383 (m, sp\(^3\) C–H bend), 1221 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH\(_2\)Cl\(_2\)) \(\lambda_{\text{max}}\) (nm): 247 and 277 (log \(\varepsilon\) 5.07 and 4.71); Fluorescence (CH\(_2\)Cl\(_2\), \(\lambda_{\text{exc}}\) 376 nm) \(\lambda_{\text{ems}}\) (nm): 413, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C\(_{91}\)H\(_{61}\)F\(_4\)NO\(_4\) [M]\(^+\): 1307.5 (100%), Found: 1307.5 (100%).

Ester Hexa-OAAux-Phenyl-Br-F (228)

Hexaaryl dendrimer 186 (82.5 mg, 0.07 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (17.0 mg, 0.07 mmol, 1.0 equiv.), DCC (17.0 mg, 0.08 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH\(_2\)Cl\(_2\) (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO\(_2\), hexane/CH\(_2\)Cl\(_2\) = 1:1) afforded 228 (64.3 mg, 65%) as a pale yellow powder.

**TLC** \(R_f = 0.38\) (hexane/CH\(_2\)Cl\(_2\) = 1:2);
**melting point** = 227-228 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: 0.81 (d, 6.8 Hz, 3H, H-83), 1.00 (d, 6.8 Hz, 3H, H-82), 2.56-2.68 (m, 1H, H-81), 4.37 (d, 8.4 Hz, 1H, H-81), 4.90-5.06 (m, 4H), 6.29-6.38 (m, 2H), 6.43 (t, 1.4 Hz, \(^1\)H, H-40), 6.50-7.06 (m, 42H), 7.74-7.77 (m, 2H, H-87/88) and 7.85-7.88 (m, 2H, H-86/89); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: 19.3 (C-83), 20.7 (C-82), 28.3 (C-81), 57.5 (C-80), [(113.7 (d, \(^2J_{C-F} = 20.8\) Hz), 113.8 (d, \(^2J_{C-F} = 20.8\) Hz)), Ar-CH], [(119.7, 119.8), C–Br], [(122.3, 122.4), 123.6 (C-86/89), 125.3, 125.3, 125.5, 125.6, 125.8, 126.6, 126.6, 126.7, 126.7, 126.8, 126.8, 126.9, 127.1, 127.2, 127.2, 127.3, 127.4, 127.5, 130.0, 130.0, 131.1, 131.1, 131.1, 131.2, 131.2, 131.3, 131.5, 131.5, 131.6, 131.8 (C-85/90), 132.6, 132.7, 132.7, 132.8, 132.9, 133.0,
**Experimental**

133.0, 133.1, 134.3 (C-87/88)), Ar-CH], [(136.5 ($d$, $4^{1}J_{CF} = 3.6$ Hz), 136.6 ($d$, $4^{1}J_{CF} = 3.7$ Hz), 138.3, 138.6, 138.9, 139.0, 139.2, 139.4, 139.5, 139.6, 139.7, 139.8, 139.9, 140.0, 140.2, 140.3, 140.5, 140.6, 140.7, 140.8, 140.9), quarternary Ar-C], 148.1 (C-1), [(160.6 ($d$, $1^{1}J_{CF} = 243.8$ Hz), 160.7 ($d$, $1^{1}J_{CF} = 243.1$ Hz)), C–F], 165.8 (C-79) and 167.5 (C-84/91); $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -117.12, -117.11 and -117.02; FTIR (neat) $\nu_{max}$ (cm$^{-1}$): [3055, 3026 (w, Ar C–H stretch)], [2964, 2928, 2872 (w, sp$^{3}$ C–H stretch)], [1767 (m), 1719 (s) (C=O stretch)], [1602, 1510, 1493 (m, Ar C=C stretch)], 1383 (m, sp$^{3}$ C–H bend), 1221 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1071 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{max}$ (nm): 250 and 280 (log $\varepsilon$ 5.10 and 4.72); Fluorescence (CH$_2$Cl$_2$, $\lambda_{exc}$ 376 nm) $\lambda_{ems}$ (nm): 413, 436 and 462; MALDI-TOF-MS (DCTB) Calcd for C$_{91}$H$_{61}$Br$_2$F$_2$NO$_4$ [M]$^+$: 1429.3 (100%), Found: 1429.3 (100%).

**Ester Hexa-OAAux-(4-Fluorophenyl)-Br-Br (229)**

Hexaaryl dendrimer 170 (99.0 mg, 0.07 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (18.0 mg, 0.07 mmol, 1.0 equiv.), DCC (18.0 mg, 0.09 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO$_2$, hexane/CH$_2$Cl$_2$ = 1:1) afforded 229 (61.3 mg, 53%) as a pale yellow powder.

**TLC** $R_f = 0.29$ (hexane/CH$_2$Cl$_2$ = 1:1); melting point = 206-207 °C; $^{1}$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.81-0.83 (m, 3H, H-83), 0.99-1.04 (m, 3H, H-82), 2.55-2.65 (m, 1H, H-81), 4.37-4.44 (m, 1H, H-80), 5.44 (ddd, 2.4, 5.6 and 8.3 Hz, 0.61H), 5.77-5.99 (m, 3.35H), 6.25-7.02 (m, 42H), 7.14-7.17 (m, 0.77H), 7.74-7.78 (m, 2H, H-87/88) and 7.84-7.87 (m, 2H, H-86/89); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(19.3, 19.3, 19.4, 20.7, 20.7), C-82/83], [(28.5, 28.5, 28.6, C-81], [(57.1, 57.3, 57.5, C-80], [(113.3, 113.5, 113.6, 113.8, 113.8, 113.9, 114.0, 114.1, 114.1, 114.2, 114.3, 114.3, 114.3, 114.3, Ar-CH], [(119.8, 119.9, C–Br], [(122.5, 122.6, 123.6 (C-86/89), 125.6, 125.7, 125.9, 125.9, 126.0, 126.8, 127.0, 127.0, 127.1, 127.1, 127.3, 127.3, 127.4, 127.4, 127.6, 130.0, 130.1, 131.0, 131.0,
Experimental

131.1, 131.2, 131.2, 131.3, 131.3, 131.4, 131.5, 131.6, 131.7, 131.8, 132.8, 132.8, 132.9, 132.9, 133.0, 134.3, 134.4), Ar-CH], [(135.5, 135.5, 135.8, 135.8, 136.2, 136.3, 138.6, 138.7, 139.2, 139.3, 139.4, 139.4, 139.5, 139.5, 139.6, 139.7, 139.8, 139.9, 139.9, 140.0, 140.1, 140.2, 140.3, 140.3, 140.5, 140.5, 140.7, 140.9, 141.0, 141.0), quarternary Ar-C], [(148.3, 148.4), C–O], [(159.4, 159.6, 159.7, 161.9, 162.0), C–F], [(165.9, 165.9, 166.0), C(O)=O], [(167.5, 167.6, 167.6), C(N)=O]; 19F NMR (470 MHz, CDCl3) δ ppm: -117.16, -116.80, -116.78 and -116.53; FTIR (neat) νmax (cm⁻¹): [3080, 3053, 3026 (w, Ar C–H stretch)], [2962, 2925, 2851 (w, sp³ C–H stretch)], [1773 (m), 1718 (s) (C=O stretch)], [1598, 1580, 1508, 1492 (m, Ar C=C stretch)], 1383 (m, sp³ C–H bend), 1263, 1221 (m, Ar C–F stretch), 1175 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH2Cl2) λmax (nm): 244, 282 and 301 (log ε 5.05, 4.83 and 4.50); Fluorescence (CH2Cl2, λexc 376 nm) λems (nm): 413, 437 and 464; nESI-MS Calcd for C91H63Br4F2N2O4 [M+NH4]+: 1605.1463 (100%), Found: 1605.1466 (100%) (Result also overlaps with [M+Na]+ species; see Appendix A for full isotope distribution).

Ester Hexa-OAux-(4-Fluorophenyl)-Br-F (230)

Hexaaryl dendrimer 188 (96.1 mg, 0.08 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (19.2 mg, 0.08 mmol, 1.0 equiv.), DCC (19.2 mg, 0.09 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH2Cl2 (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO2, hexane/CH2Cl2 = 1:1) afforded 230 (61.1 mg, 54%) as a pale yellow powder.

TLC Rf = 0.58 (hexane/CH2Cl2 = 1:2); melting point = 218-219 °C; 1H NMR (400 MHz, CDCl3) δ ppm: 0.81-0.84 (m, 3H, H-83), 0.99-1.05 (m, 3H, H-82), 2.54-2.66 (m, 1H, H-81), 4.38-4.44 (m, 1H, H-80), 5.43-5.49 (m, 0.61H), 5.80-6.01 (m, 3H), 6.26-7.07 (m, 44H), 7.14-7.17 (m, 0.77H), 7.74-7.78 (m, 2H, H-87/88) and 7.84-7.87 (m, 2H, H-86/89); 13C NMR (100 MHz, CDCl3) δ ppm: [(19.3, 19.3, 19.4, 20.7, 20.7), C-82/83], [(28.5, 28.5, 28.6, C-81)], [(57.1, 57.3, 57.6), C-80], [(113.2, 113.4, 113.5, 113.6, 113.6, 113.6, 113.6, 113.7, 113.8, 113.8, 113.8, 113.9, 113.9, 113.9, 114.0, 114.0, 114.1, 114.1, 114.2, 114.2, 114.3, 114.3, 114.3,
114.3, 114.4, 114.5, 114.5, 114.5), Ar-CH], [(119.8, 119.9), C–Br], [(122.5, 122.5, 122.6, 122.6, 123.6 (C-86/89), 125.4, 125.5, 125.6, 125.7, 125.7, 125.9, 126.0, 126.7, 126.8, 126.9, 127.0, 127.0, 127.1, 127.1, 127.2, 127.3, 127.4, 127.4, 127.5, 127.5, 127.6, 130.0, 130.1, 131.0, 131.1, 131.2, 131.2, 131.3, 131.3, 131.4, 131.4, 131.5, 131.5, 131.5, 131.6, 131.6, 131.6, 131.7, 131.8, 132.2, 132.3, 132.3, 132.5, 132.5, 132.6, 132.6, 132.8, 132.8, 132.9, 133.0, 133.1, 133.1, 133.2, 133.2, 133.3, 133.3 (C-87/88), Ar-CH], [(135.5, 135.5, 135.6, 135.7, 135.8, 135.9, 135.9, 136.0, 136.0, 136.3, 136.4, 136.4, 136.4, 138.4, 138.4, 138.6, 138.7, 138.7, 139.1, 139.2, 139.3, 139.3, 139.3, 139.4, 139.5, 139.5, 139.6, 139.6, 139.7, 139.7, 139.7, 139.8, 139.9, 139.9, 140.0, 140.0, 140.1, 140.1, 140.2, 140.2, 140.2, 140.3, 140.3, 140.4, 140.4, 140.5, 140.5, 140.5, 140.5, 140.6, 140.6, 140.6, 140.7, 140.7, 140.7, 140.9, 140.9, 140.9, 140.9, 141.0, 141.1, 141.1, 141.2), quarternary Ar-C], [(148.3, 148.3, 148.4), C–O], [(159.4, 159.4, 159.4, 159.5, 159.6, 159.6, 159.7, 159.7, 161.8, 161.9, 161.9, 162.0, 162.1, 162.1), C–F], [(165.9, 166.0, 166.0), C(O)=O], [(167.5, 167.5, 167.6), C(N)=O]; $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ ppm: -117.28, -117.19, -116.98, -116.98, -116.97, -116.97, -116.92, -116.89, -116.87, -116.86, -116.86, -116.82, -116.81, -116.65 and -116.53; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3054, 3026 (w, Ar C–H stretch)], [2963, 2928, 2874 (w, sp$^3$ C–H stretch)], [1768 (m), 1720 (s) (C=O stretch)], [1602, 1510 (m, Ar C=C stretch)], 1383 (m, sp$^3$ C–H bend), 1220 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$, $\lambda_{\text{max}}$ (nm): 248 and 278 (log $\varepsilon$ 5.08 and 4.73); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 438 and 462; MALDI-TOF-MS (DCTB) Calcd for C$_{91}$H$_{59}$Br$_2$F$_4$NO$_4$ [M]$^+$: 1465.3 (100%), Found: 1465.3 (100%).

**Ester Hexa-OAux-(2-Fluorophenyl)-Br-Br (231)**

Hexaaryl dendrimer 173 (98.0 mg, 0.07 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (18.0 mg, 0.07 mmol, 1.0 equiv.), DCC (18.0 mg, 0.09 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO$_2$, hexane/CH$_2$Cl$_2$ = 1:1) afforded 231 (54.9 mg, 48%) as a pale yellow powder.
TLC $R_f = 0.23$ (hexane/CH$_2$Cl$_2$ = 1:1); melting point = 276-277 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 0.80-0.88 (m, 3H, H-83), 0.95-1.05 (m, 3H, H-82), 2.54-2.69 (m, 1H, H-81), 4.31-4.47 (m, 1H, H-80), 5.30-5.45 (m, 1H), 5.49-5.55 (m, 0.32H), 5.61 ($d$, 7.5 Hz, 0.09H), 5.72 ($td$, 1.4 and 7.5 Hz, 0.14H), 5.84-6.13 (m, 2H), 6.18-6.29 (m, 0.68H), 6.34-7.23 (m, 43H), 7.74-7.77 (m, 2H, H-87/88) and 7.85-7.89 (m, 2H, H-86/89); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: [(19.2, 19.2, 19.4, 19.5, 20.7, 20.7), C-82/83], [(28.2, 28.2, 28.3, 28.4, 28.5, 28.5, 28.6), C-81], [(57.1, 57.2, 57.2, 57.3, 57.4, 57.8, 57.8), C-80], [(114.3, 114.4, 114.4, 114.5, 114.5, 114.6, 114.6, 114.9, 114.9, 119.8, 119.9, 121.6, 121.9, 121.9, 122.0, 122.2, 122.3, 122.5, 122.6, 122.6, 123.0, 123.1, 123.1, 123.2, 123.2, 123.2, 123.3, 123.3, 123.3, 123.4, 123.4, 123.5, 123.5, 123.6, 123.6, 123.7, 125.3, 125.3, 125.4, 125.6, 125.6, 125.7, 125.8, 125.9, 126.1, 126.1, 126.2, 126.2, 126.3, 126.3, 126.4, 126.5, 126.5, 126.6, 126.7, 126.8, 126.9, 126.9, 127.0, 127.0, 127.1, 127.2, 127.2, 127.3, 127.3, 127.4, 127.5, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 127.8, 128.1, 128.1, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.9, 128.9, 129.0, 130.0, 130.0, 130.1, 130.1, 130.4, 130.4, 130.5, 130.6, 130.6, 130.6, 130.6, 130.7, 130.7, 130.8, 130.9, 130.9, 130.9, 131.0, 131.0, 131.0, 131.3, 131.4, 131.4, 131.4, 131.5, 131.6, 131.6, 131.7, 131.7, 131.7, 131.8, 131.8, 131.8, 131.8, 131.9, 131.9, 131.9, 132.7, 132.7, 132.7, 132.8, 132.8, 132.9, 133.0, 133.0, 133.1, 133.1, 133.1, 134.1, 134.3, 134.3, 134.3, 134.4, 134.5, 134.5, 134.6, 134.7, 134.8, 134.9), Ar-CH], [(138.9, 138.9, 138.9, 139.0, 139.1, 139.2, 139.2, 139.2, 139.3, 139.3, 139.3, 139.3, 139.4, 139.4, 139.5, 139.5, 139.5, 139.6, 139.6, 139.7, 139.7, 139.7, 139.8, 139.9, 139.9, 139.9, 140.0, 140.0, 140.1, 140.1, 140.1, 140.2, 140.3, 140.3, 140.4, 140.5, 140.6, 140.7, 140.7, 140.8, 141.4, 141.4, 141.4, 141.5, 141.5, 141.6, 141.6, 141.7, 141.7), quarternary Ar-C], [(148.2, 148.3, 148.4, 148.4, 148.5, 148.5, 148.6), C–O], [(158.2, 158.2, 158.3, 158.3, 158.4, 158.4, 158.5, 158.5, 158.5, 158.7, 158.7, 160.5, 160.6, 160.7, 160.8, 160.8, 160.9, 160.9, 161.0, 161.0, 161.1), C–F], [(165.7, 165.7, 165.8, 165.9), C(O)=O], [(167.4, 167.5, 167.6), C(N)=O]; $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ ppm: -112.43, -112.35, -112.15, -112.10, -112.08, -112.01, -112.00, -111.95, -111.58, -111.40, -111.37, -111.32, -111.20, -110.95, -110.89 and -110.82; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3079, 3055, 3027 (w, Ar C–H stretch)], [2963, 2927, 2873 (w, sp$^3$ C–H stretch)], [1767 (m), 1719 (s) (C=O stretch)], [1583, 1491 (m, Ar C=C stretch)], 1383 (m, sp$^3$ C–H bend), 1227 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$
(nm): 248 and 278 (log ε 5.09 and 4.71); Fluorescence (CH₂Cl₂, λ_{exc} 376 nm) λ_{ems} (nm): 413, 437 and 464; MALDI-TOF-MS (DCTB) Calcd for C₉₁H₉₉Br₂F₄NO₄ [M⁺]: 1587.1 (100%), Found: 1587.1 (100%).

**Ester Hexa-OAaux-(2-Fluorophenyl)-Br-F (232)**

Hexaaryl dendrimer 190 (103.2 mg, 0.08 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (21.0 mg, 0.08 mmol, 1.0 equiv.), DCC (21.0 mg, 0.10 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH₂Cl₂ (1 mL) were treated as described in General Procedure F. Purification by preparative TLC (SiO₂, hexane/CH₂Cl₂ = 1:1) afforded 232 (57.8 mg, 47%) as a pale yellow powder.

TLC R_{f} = 0.48 (hexane/CH₂Cl₂ = 1:2); melting point = 256-257 °C; ¹H NMR (400 MHz, CDCl₃) δ ppm: 0.80-0.85 (m, 3H, H-83), 0.95-1.05 (m, 3H, H-82), 2.52-2.71 (m, 1H, H-81), 4.31-4.48 (m, 1H, H-80), 5.31-5.56 (m, 1.38H), 5.60-5.65 (m, 0.09H), 5.69-5.75 (m, 0.14H), 5.89-7.23 (m, 47H), 7.75-7.78 (m, 2H, H-87/88) and 7.85-7.90 (m, 2H, H-86/89); ¹³C NMR (100 MHz, CDCl₃) δ ppm: [(19.2, 19.3, 19.4, 19.5, 19.6, 20.7, 20.7), C-82/83], [(28.2, 28.2, 28.4, 28.5, 28.6), C-81], [(57.2, 57.2, 57.5, 57.8, 57.8, 57.8), C-80], [(113.6, 113.7, 113.7, 113.8, 113.8, 113.9, 114.0, 114.0, 114.4, 114.4, 114.6, 114.6, 114.6, 114.7, 114.7, 114.9, 119.8, 119.9, 122.5, 122.5, 122.6, 122.6, 123.0, 123.1, 123.2, 123.2, 123.4, 123.4, 123.6, 123.6, 123.7, 125.2, 125.3, 125.4, 125.4, 125.5, 125.5, 125.6, 125.6, 125.7, 125.7, 125.8, 125.8, 125.8, 125.9, 126.2, 126.2, 126.2, 126.2, 126.3, 126.3, 126.3, 126.4, 126.5, 126.5, 126.5, 126.6, 126.6, 126.7, 126.8, 126.8, 126.9, 126.9, 127.0, 127.0, 127.1, 127.1, 127.2, 127.2, 127.3, 127.3, 127.4, 127.4, 127.5, 127.5, 127.6, 128.1, 128.1, 128.2, 128.2, 128.3, 128.3, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.8, 128.8, 128.8, 128.9, 129.9, 130.0, 130.0, 130.0, 130.1, 130.2, 130.4, 130.5, 130.5, 130.6, 130.6, 130.7, 130.7, 130.8, 130.8, 130.9, 131.0, 131.1, 131.3, 131.3, 131.4, 131.4, 131.5, 131.5, 131.5, 131.6, 131.6, 131.7, 131.8, 131.8, 131.8, 131.9, 131.9, 132.0, 132.0, 132.0, 132.3, 132.4, 132.4, 132.5, 132.5, 132.5, 132.5, 132.6, 132.6, 132.6, 132.7, 132.7, 132.8, 132.8, 132.9, 133.0, 133.0, 134.3, 134.3, 134.3, 134.6), Ar-CH] [(136.2, 136.2, 136.3, 136.3, 136.3, 136.4, 136.4, 136.4, 136.4, 136.5, 136.5, 136.5, 136.5, 138.8, 138.9, 138.9, 139.0, 139.0, 139.1, 139.1, 139.2, 139.2, 139.2, 139.3, 139.3, 139.4, 139.5, 139.5,
Experimental

139.5, 139.6, 139.7, 139.7, 139.8, 139.8, 139.9, 139.9, 140.0, 140.0, 140.1, 140.1, 140.2, 140.2, 140.2, 140.3, 140.3, 140.4, 140.4, 140.6, 140.6, 140.7, 140.7, 140.8, 140.8, 140.9, 140.9, 141.0, 141.4, 141.5, 141.6, 141.7, 141.7, 141.8, 141.9), quaternary Ar-C] [(148.2, 148.4, 148.5), C–O)], [(158.2, 158.2, 158.3, 158.3, 158.4, 158.4, 158.4, 158.5, 158.5, 158.7, 160.6, 160.7, 160.7 (1J_C-F = 243.6 Hz), 160.7 (1J_C-F = 243.7 Hz), 160.7, 160.8, 160.8, 160.8, 160.9, 160.9, 161.1, 161.1, 161.1, 161.2, 161.2), C–F], [(165.7, 165.7, 165.8, 165.9), C(O)=O], [(167.4, 167.5, 167.6, 167.6), C(N)=O];

19F NMR (470 MHz, CDCl3) δ ppm: -117.08, -117.08, -117.03, -117.02, -116.99, -116.99, -116.97, -116.96, -116.95, -116.94, -116.93, -116.92, -116.91, -116.90, -116.90, -116.89, -116.88, -116.88, -116.87, -116.87, -116.84, -116.44, -116.37, -112.36, -112.19, -112.14, -112.13, -112.10, -112.08, -112.07, -112.03, -112.02, -112.00, -111.97, -111.95, -111.61, -111.60, -111.42, -111.40, -111.39, -111.36, -111.33, -111.24, -111.22, -110.96 (ABq, ΔδAB = 9.79 Hz, JAB = TS JF-F = 4.5 Hz), -110.90 (ABq, ΔδAB = 5.99 Hz, JAB = TS JF-F = 4.5 Hz), -110.83 and -110.82; FTIR (neat) νmax (cm⁻¹): [3080, 3055, 3027 (w, Ar C–H stretch)], [2962, 2926, 2873 (w, sp3 C–H stretch)], [1769 (m), 1720 (s) (C=O stretch)], [1603, 1584, 1511, 1493 (m, Ar C=C stretch)], 1383 (m, sp3 C–H bend), 1226 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1071 (m, Ar C–Br stretch);

UV/Vis (CH2Cl2) λmax (nm): 245 and 278 (log ε 5.43 and 4.96); Fluorescence (CH2Cl2, λexc 376 nm) λems (nm): 412, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C91H59Br2F4NO4 [M]⁺: 1465.3 (100%), Found: 1465.3 (100%).

6.9 Synthesis of Ester of Hexaaryl Dendrimer Monoadducts

Monoadduct Ester MonoHexa-OAAux-(4-Fluorophenyl)-Br (233)

Hexaaryl dendrimer monoadduct 181 (73.8 mg, 0.09 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (21.6 mg, 0.09 mmol, 1.0 equiv.), DCC (21.6 mg, 0.11 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH2Cl2 (1 mL) were treated as described in General Procedure F. Purification by reverse-phase HPLC (ACN 100%) afforded 233 (83.3 mg, 89%) as a pale yellow powder.
Experimental

TLC $R_f = 0.28$ (hexane/CH$_2$Cl$_2$ = 1:1); melting point = 168-169 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.94 (d, 6H, H-55), 1.14-1.16 (m, 6H, H-54), 2.69-2.78 (m, 2H, H-53), 4.69 (d, 2H, H-52), 6.48 (td, 2.7 and 8.8 Hz, 1H), 6.54-6.64 (m, 5H), 6.66-6.70 (m, 8H), 6.73-6.94 (m, 28H), 6.97-7.04 (m, 12H), 7.35-7.40 (m, 4H), 7.75-7.80 (m, 4H, H-59/60) and 7.87-7.93 (m, 4H, H-58/61);

$^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(19.3, 19.4, 20.9, C-54/55)], 29.1 (C-53), [(57.3, 57.3), C-52], [(88.1, 88.1, 88.6), C≡C], [(114.0, 114.0, 114.2, 114.2, 114.3, 114.4, 115.6, 115.8), Ar-CH], [(119.2, 119.2), C–Br], [(120.0, 121.8, 121.8, 122.9, 123.8 (C-58/61), 125.0, 125.1, 125.9, 126.1, 126.1, 127.2, 127.2, 127.2, 127.3, 127.4, 130.2, 130.3, 131.0, 131.1, 131.2, 131.2), Ar-CH], 131.8 (C-57/62), [(131.8, 132.5, 132.5, 132.6, 132.7, 132.8, 132.8, 132.9, 132.9, 133.5, 133.6, 134.5 (C-59/60), Ar-CH], 135.5, 135.6, 135.6, 139.1, 139.1, 139.1, 139.2, 139.2, 139.3, 139.3, 139.3, 139.3, 139.3, 139.6, 139.8, 139.8, 139.8, 139.9, 140.5, 140.6, 140.8, 140.8, 141.9, 141.9, 141.9), quarternary Ar-C], [(149.2, 149.2), C–O], [(160.9 (1C-F = 243.9 Hz), 161.0 (1C-F = 243.9 Hz), 162.6 (1C-F = 248.3 Hz), C–F)] [(166.9, 166.9), C(O)=O], [(167.7, 167.8), C(N)=O];

$^{19}$F NMR (470 MHz, CDCl$_3$) δ ppm: -116.47, -116.45 and -110.74; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): 3054 (w, Ar C–H stretch), [2958, 2921, 2850 (m, sp$^3$ C–H stretch)], [1773 (m), 1717 (s) (C=O stretch)], [1597, 1508 (m, Ar C=C stretch)], 1383 (m, sp$^3$ C–H bend), 1220 (m, Ar C–F stretch), 1175 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 241, 283 and 300 (log $\varepsilon$ 4.91, 4.73 and 4.50); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 437 and 462; MALDI-TOF-MS (DCTB) Calcd for C$_{63}$H$_{41}$Br$_2$F$_2$NO$_4$ [M]$^{+}$: 1073.1 (100%), Found: 1073.1 (100%).

Monoadduct Ester MonoHexa-OAaux-(2-Fluorophenyl)-Br (234)
Hexaaryl dendrimer monoadduct 183 (71.9 mg, 0.09 mmol, 1.0 equiv.), (S)-2-(1,3-dioxoindolin-2-yl)-3-methylbutanoic acid (21.0 mg, 0.09 mmol, 1.0 equiv.), DCC (21 mg, 0.10 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by reverse-phase HPLC (ACN 100%) afforded 234 (76.0 mg, 83%) as a pale yellow powder.
Experimental

TLC $R_f = 0.28$ (hexane/CH$_2$Cl$_2 = 1:1$); melting point = 191-192 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 0.94 (d, 6.8 Hz, 12H, H-54), 1.14-1.17 (m, 12H, H-55), 2.69-2.80 (m, 4H, H-53), 4.67-4.70 (m, 4H, H-52), 6.41-6.46 (m, 1H), 6.54-6.98 (m, 83H), 7.01-7.10 (m, 24H), 7.25-7.30 (m, 4H), 7.36-7.41 (m, 4H), 7.75-7.80 (m, 8H, H-59/60), 7.88-7.94 (m, 8H, H-58/61); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(19.4, 19.4, 20.9, 20.9), C-54/55], [(29.0, 29.0), C-53], [(57.3, 57.3, 57.3, 57.4), C-52], [(82.9, 82.9, 82.9, 82.9, 83.0, 83.0, 83.0, 83.0, 83.4, 93.4, 93.4, 93.4, 93.5, 93.5, 93.5), C=C], [(111.7, 111.7, 111.9, 111.9, 114.4, 114.4, 114.4, 114.5, 114.6, 114.6, 114.7, 114.7, 115.0, 115.0, 115.5, 115.7, 120.0, 122.0, 122.2, 122.2, 122.3, 122.4, 122.8, 122.9, 122.9, 123.0, 123.0, 123.1, 123.1, 123.2, 123.2, 123.2, 123.7, 123.8, 124.0, 124.0, 124.0, 124.2, 124.4, 124.8, 126.1, 126.2, 126.2, 126.7, 126.8, 126.8, 126.8, 127.1, 127.2, 127.2, 127.3, 127.3, 127.3, 127.3, 127.4, 127.4, 127.4, 127.5, 127.5, 127.6, 127.6, 127.8, 128.8, 128.8, 128.9, 128.9, 129.0, 130.1, 130.2, 130.2, 130.2, 130.2, 130.3, 130.3, 130.3, 130.4, 130.4, 130.4, 130.4, 130.7, 130.8, 131.0, 131.0, 131.0, 131.0, 131.1, 131.1, 131.2, 131.2, 131.3, 131.3, 131.4, 131.5, 131.7, 131.8, 131.8, 131.8, 131.8, 132.4, 132.4, 132.4, 132.5, 132.5, 132.6, 132.6, 132.8, 132.9, 133.5, 134.4, 134.5, 135.0, 135.0, 135.1, 135.1), Ar-CH], [(139.0, 139.0, 139.0, 139.0, 139.1, 139.1, 139.1, 139.2, 139.2, 139.2, 139.2, 139.5, 139.5, 139.5, 139.5, 139.5, 139.6, 139.6, 139.6, 139.6, 139.7, 139.7, 139.7, 140.4, 140.4, 140.5, 140.5, 140.5, 140.5, 141.7, 141.3, 141.3, 141.4, 141.4, 141.6, 141.6, 141.6, 141.7), quarternary Ar-C], [(148.9, 149.0, 149.2, 149.3), C–O], [(159.4 ($^1$J$_{C-F} = 242.3$ Hz), 162.6 ($^1$J$_{C-F} = 250.3$ Hz), 162.7 ($^1$J$_{C-F} = 250.6$ Hz), C–F], [(166.7, 166.8, 166.9), C(O)=O], [(167.7, 167.7), C(N)=O]; $^{19}$F NMR (470 MHz, CDCl$_3$) δ ppm: -112.14, -112.01, -111.75, -111.72, -109.80, -109.79, -109.69 and -109.69; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3057, 3031 (w, Ar C–H stretch)], [2964, 2925 (w, sp$^3$ C–H stretch)], [1771 (m), 1716 (s) (C=O stretch)], [1601, 1580, 1492 (m, Ar C=C stretch)], 1383 (m, sp$^3$ C–H bend), 1213 (m, Ar C–F stretch), 1174 (m, C–O stretch) and 1071 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 240, 282 and 305 (log $\varepsilon$ 4.90, 4.67 and 4.48); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{em}}$ (nm): 414, 437 and 463; MALDI-TOF-MS (DCTB) Calcd for C$_{63}$H$_{41}$Br$_2$F$_2$NO$_4$ [M]$^+$: 1073.1 (100%), Found: 1073.1 (100%).
6.10 Focal Expansions – Synthesis of Ester Unit

Dendrimer Penta-OVal-Br-Br (236)

Pentaaryl dendrimer 153 (66.5 mg, 0.0568 mmol, 1.0 equiv.), 5-bromovaleric acid (10.3 mg, 0.0569 mmol, 1.0 equiv.), DCC (14.1 mg, 0.0682 mmol, 1.2 equiv.), DMAP (catalytic) and anhydrous CH$_2$Cl$_2$ (1 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 6:1) afforded 236 (48.0 mg, 63%) as a pale yellow powder.

TLC $R_f$ = 0.55 (hexane/EtOAc = 4:1); melting point = 198-199 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 1.73-1.80 (m, 2H, H-69), 1.83-1.91 (m, 2H, H-70), 2.40 (t, 8 Hz, 2H, H-68), 3.39 (t, 8 Hz, 2H, H-71), 6.57-6.59 (m, 6H, H-2/22/24/55/57/36), 6.65-6.71 (m, 8H, H-15/17/29/31/48/50/62/64), 6.87-6.95 (m, 7H, H-28/30/32/34/61/63/65), 7.01 (d, 8.0 Hz, 4H, H-21/25/54/58), 7.06-7.09 (m, 8H, H-8/10/14/18/41/43/47/51) and 7.19-7.22 (m, 8H, H-7/9/11/33/40/44/46); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 23.6 (C-69), 31.8 (C-70), 33.0 (C-71), 33.3 (C-68), 120.0 (C-23/56), 120.3 (C-16/49), 121.3 (C-2/36), 126.3 (C-30/63), 126.7 (C-9/42), 127.5 (C-28/32/61/65), 127.9 (C-7/11/40/44), 129.3 (C-34), 130.0 (C-8/10/41/43), 130.5 (C-14/18/47/51), 131.4 (C-29/31/62/64), 131.8 (C-33/66), 133.0 (C-22/24/55/57), 133.1 (C-15/17/48/50), [(138.1, 138.4, 139.0, 139.2, 139.9, 140.3, 141.0, 141.1, 142.2, quarternary Ar-C], 149.4 (C-1) and 171.3 (C-67); FTIR (neat) $\nu$$_{max}$ (cm$^{-1}$): [3049, 3024 (w, Ar C–H stretch)], [2956, 2925, 2853 (w, $sp^3$ C–H stretch)], 1759 (m, C=O stretch), [1600, 1587, 1488 (m, Ar C=C stretch)], 1388 (m, $sp^3$ C–H bend), 1177 (m, C–O stretch) and 1072 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda$$_{max}$ (nm): 254 and 280 (log $\varepsilon$ 5.20 and 4.86); Fluorescence (CH$_2$Cl$_2$, $\lambda$$_{exc}$ 376 nm) $\lambda$$_{ems}$ (nm): 413, 438 and 464; MALDI-TOF-MS [M+Na]$^+$ (dithranol) m/z = 1350.4 (8%), 1351.4 (6%), 1352.4 (43%), 1353.4 (29%), 1354.4 (89%), 1355.4 (58%), 1356.4 (100%), 1357.4 (57%), 1358.4 (54.4%), 1359.4 (28%), 1360.4 (16%), 1361.4 (6%), 1362.4 (2%) and 1363.4 (2%).

Dendrimer Penta-OVal-F-F (237)

Pentaaryl dendrimer 154 (0.3000 g, 0.32 mmol, 1.0 equiv.), 5-bromovaleric acid (0.0590 g, 0.32 mmol, 1.0 equiv.), DCC (0.0800 g, 0.39 mmol, 1.2 equiv.), DMAP
(catalytic) and anhydrous CH$_2$Cl$_2$ (5 mL) were treated as described in General Procedure F. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 95:5 to 80:20) afforded 237 (0.2327 g, 66%) as a yellow powder.

\[ \text{TLC } R_f = 0.23 \text{ (hexane/EtOAc = 9:1); melting point} = 169-170 \degree C; \]

$^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 1.74-1.81 (m, 2H, H-69), 1.85-1.92 (m, 2H, H-70), 2.41 (t, 7.2 Hz, 2H, H-68), 3.40 (t, 6.4 Hz, 2H, H-71), 6.56-6.61 (m, 6H, H-2/22/24/36/55/57), 6.63-6.69 (m, 8H, H-15/17/21/25/48/50/54/58), 6.73-6.78 (m, 8H, H-14/18/29/31/47/51/62/64), 6.87-6.95 (m, 7H, H-28/30/32/34/61/63/65), 7.09-7.11 (m, 4H, H-8/10/41/43), 7.16-7.23 (m, 6H, H-7/9/11/40/42/44) and 7.24 (s, 2H, H-33/66);

$^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 23.6 (C-69), 31.9 (C-70), 33.0 (C-71), 33.3 (C-68), 114.0 (d, $^2$J$_{C-F}$ = 21.1 Hz, H-22/24/55/57), 114.3 (d, $^2$J$_{C-F}$ = 21.1 Hz, H-15/17/48/50), 121.2 (C-2/36), 126.2 (C-30/63), 126.6 (C-9/42), 127.4 (C-28/32/61/65), 127.8 (C-7/11/40/44), 129.3 (C-34), 130.1 (C-8/10/41/43), 131.5 (C-29/31/62/64), 131.6 (C-33/66), 132.9 (d, $^3$J$_{C-F}$ = 7.9 Hz, H-21/25/54/58), 133.0 (d, $^3$J$_{C-F}$ = 7.9 Hz, H-14/18/47/51), 135.8 (d, $^4$J$_{C-F}$ = 3.4 Hz, C-13/46), 136.1 (d, $^4$J$_{C-F}$ = 3.4 Hz, H-20/53), [(138.7, 139.4, C-139.5, 139.8, 140.8, 141.2, 141.3, 142.3), quarternary Ar-C], 149.4 (C-1), 160.9 (d, $^1$J$_{C-F}$ = 243.9 Hz, C-23/56), 161.1 (d, $^1$J$_{C-F}$ = 243.8 Hz, C-16/49) and 171.3 (C-67); $^{19}$F NMR (376 MHz, CDCl$_3$) δ ppm: -116.73 and -116.43; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3055, 3026 (w, Ar C–H stretch)], [2961, 2934 (w, sp$^3$ C–H stretch)], 1759 (m, C=O stretch), [1603 (m), 1510 (s) (Ar C=C stretch)], 1378 (m, sp$^3$ C–H bend), 1220 (m, Ar C–F stretch) and 1178 (m, C–O stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 251 and 278 (log e 5.11 and 4.79); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 436 and 465; MALDI-TOF-MS (dithranol) Calcd for C$_{71}$H$_{49}$BrF$_4$O$_2$Na [M+Na]$^+$: 1113.3 (100%), Found: 1113.5 (100%).

**6.11 Periphery Expansions – Pendant Dendrimers**

1-Bromo-3-(2-phenylethynyl)benzene (245)$^{151}$

3-Bromoiiodobenzene (1.89 mL, 15 mmol), phenylpropionic acid (2.6280 g, 18 mmol), CuI (0.0600 g, 0.3 mmol), PPh$_3$ (0.1572 g, 0.6 mmol) and K$_2$CO$_3$ (4.1400 g, 30 mmol) were added into a round bottom flask. The flask was evacuated and backfilled with
nitrogen gas (3 cycles). Water (90 mL) was added and the flask was once again evacuated and backfilled with nitrogen gas (3 cycles). The mixture was heated to 100 °C and left stirring for 48 h. The resulting mixture was then cooled to room temperature and extracted with EtOAc. The organic fractions were combined, dried (MgSO₄), filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (SiO₂, hexane) to obtain 245 (1.8728 g, 49%) as a colourless liquid.

**TLC** R<sub>f</sub> = 0.53 (hexane); **¹H NMR** (400 MHz, CDCl₃) δ ppm: 7.22 (t, 8.0 Hz, 1H, H-13), 7.35-7.39 (m, 3H, H-2/3/4), 7.45-7.49 (m, 2H, H-12/14), 7.53-7.55 (m, 2H, H-1/5) and 7.70 (t, 1.6 Hz, 1H, H-10); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 87.9 (C-8), 90.8 (C-7), 122.3 (C-9), 122.9 (C-6), 125.4 (C-11), 128.5 (C-2/4), 128.8 (C-3), 129.9 (C-13), 130.3 (C-14), 131.5 (C-12), 131.8 (C-1/5), 134.4 (C-10); **FTIR** (neat) ν<sub>max</sub> (cm<sup>-1</sup>): 3059 (w, Ar C–H stretch), 2219 (w, C≡C stretch), [1587, 1554, 1490 (m, Ar C=C stretch)] and 1070 (m, Ar C–Br); **APCI-MS** [M+CH₃OH+H]<sup>+</sup> m/z = 289 (83%) and 291 (100%); **HRMS** Calcd for C₁₄H₉Br [M]<sup>+</sup>: 255.9882, Found: 255.9873.

Data collected matched the reported data, full NMR assignment made by the author.

1-(2-Bromophenyl)-3,4-bis(4-fluorophenyl)-2,5,6-triphenylbenzene (246)

Compound 143 (1.57 g, 3.9 mmol, 1.0 equiv.), 245 (1.50 g, 5.8 mmol, 1.5 equiv.), and anhydrous o-xylene (10 mL) was treated as described in General Procedure E at 200 °C for 42 h. Purification by flash column chromatography (SiO₂, hexane/CH₂Cl₂/toluene, 10:1:1) afforded 246 (2.23 g, 92%) as a pale yellow powder.

**TLC** R<sub>f</sub> = 0.53 (hexane); **melting point** = > 300 °C; **¹H NMR** (400 MHz, CDCl₃) δ ppm: 6.57-6.62 (m, 4H) and 6.71-7.01 (m, 23H); **¹³C NMR** (100 MHz, CDCl₃) δ ppm: 114.0 (d, <sup>2</sup>J<sub>C,F</sub> = 21.0), 120.9 (C-41), [(125.6, 125.8, 125.9, 126.9, 126.9, 127.0, 127.0, 127.1, 127.2, 128.3, 128.5, 130.0, 131.1, 131.2, 131.3, 131.4, 132.7, 132.8, 132.8, 132.8, 134.4), Ar-CH], [(136.3 (d, <sup>4</sup>J<sub>C,F</sub> = 3.6 Hz), 136.4 (d, <sup>4</sup>J<sub>C,F</sub> = 3.1 Hz), 139.2, 139.6, 140.0, 140.0, 140.4, 140.2, 140.6, 140.7, 140.8, 142.6), quarternary Ar-C]
Experimental

and 160.8 (d, $J_{C-F} = 243.4$ Hz, C–F); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -116.79 and -116.77; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3057, 3026 (w, Ar C–H stretch)], [1604, 1563, 1510 (m, Ar C=C stretch)], 1225 (m, Ar C–F stretch) and 1073 (m, Ar C–Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 245 and 276 (log $\varepsilon$ 4.52 and 4.09); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 373 nm) $\lambda_{\text{ems}}$ (nm): 413, 438 and 464; HRMS Calcd for C$_{42}$H$_{27}$BrF$_2$ [M]$^+$: 648.1259, Found: 648.1248.

I-(2-(Triisopropylsilylethynyl)phenyl)-3,4-bis(4-fluorophenyl)-2,5,6-triphenylbenzene (247)

Compound 246 (1.5332 g, 2.4 mmol, 1.0 equiv.), triisopropylsilylecetylene (0.85 mL, 3.8 mmol, 1.5 equiv.), Pd(PPh$_3$)$_2$Cl$_2$ (0.0832 g, 0.12 mmol, 5 mol%), PPh$_3$ (0.0621 g, 0.24 mmol, 10 mol%), CuI (0.0456 g, 0.24 mmol, 10 mol%), Et$_3$N (15 mL) and anhydrous toluene (15 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO$_2$, hexane/CH$_2$Cl$_2$ = 95:5 to 85:15) afforded 247 (1.3009 g, 73%) as a white powder. TLC $R_f$ = 0.33 (hexane/CH$_2$Cl$_2$ = 4:1); melting point = 224-225 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 1.07 (s, 21H, H-46/47/49/50/52/53), 1.08 (s, 21H, H-45/48/51), 6.57-6.61 (m, 4H) and 6.73-6.98 (m, 23H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 11.4 (C-45/48/51), 18.8 (C-46/47/49/50/52/53), 89.5 (C-44), 107.5 (C-43), [(113.9 (d, $J_{C-F} = 21.1$ Hz), 121.9, 125.6, 125.7, 125.7, 126.6, 126.9, 126.9, 127.0, 127.2, 128.7, 131.2, 131.2, 131.4, 131.4, 131.5, 131.5, 132.8, 132.8, 132.9, 132.9, 135.9). Ar-CH], [(136.5 (d, $J_{C-F} = 3.4$ Hz), 139.6, 139.7, 139.8, 140.2, 140.2, 140.4, 140.4, 140.7, 140.8), quarterary Ar-C], and 160.8 (d, $J_{C-F} = 243.3$ Hz, C–F); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ ppm: -116.89; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3081, 3058, 3025 (w, Ar C–H stretch)], [2941, 2891, 2864 (m, sp$^3$ C–H stretch), 2151 (w, C=C stretch), [1603, 1577, 1510 (m, Ar C=C stretch)], 1442 (m, Si–C stretch), 1391 (m, sp$^3$ C–H bend) and 1232 (m, Ar C–F stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 251 and 266 (log $\varepsilon$ 4.86 and 4.66); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 373 nm) $\lambda_{\text{ems}}$ (nm): 413, 438 and 465; ASAP-MS [M]$^+$ and [M+H]$^+$ m/z = 750 (50%), 751 (100%), 752 (50%) and 753 (10%); HRMS Calcd for C$_{53}$H$_{48}$F$_2$Si [M]$^+$: 750.3488, Found: 750.3487, and Calced for C$_{53}$H$_{48}$F$_2$Si [M+H]$^+$: 751.3566, Found: 751.3553.
Experimental

1-(2-Ethynylphenyl)-3,4-bis(4-fluorophenyl)-2,5,6-triphenylbenzene (241)

Compound 241 (1.0310 g, 1.37 mmol, 1.0 equiv.), TBAF (1.0 M in THF, 2.75 mL, 2.75 mmol, 3.0 equiv.) and anhydrous THF (3.5 mL) were treated as described in General Procedure B. Purification by flash column chromatography (SiO₂, hexane/CH₂Cl₂ = 95:5 to 85:15) afforded 241 (0.0729 g, 95%) as a white powder.

TLC R<sub>f</sub> = 0.23 (hexane/CH₂Cl₂ = 4:1); melting point = 285 °C; <sup>1</sup>H NMR (400 MHz, CDCl₃) δ ppm: 2.88 (s, 1H, H-44), 6.57-6.61 (m, 4H) and 6.76-7.00 (m, 23H); <sup>13</sup>C NMR (100 MHz, CDCl₃) δ ppm: 76.5 (C-44), 83.9 (C-43), [(113.9 (d, <sup>2</sup>J<sub>C-F</sub> = 21.1 Hz), 114.0 (d, <sup>2</sup>J<sub>C-F</sub> = 21.2 Hz), 120.5, 125.6, 125.7, 125.8, 126.8, 126.9, 126.9, 127.0, 127.0, 127.1, 129.4, 131.2, 131.2, 131.3, 131.4, 131.4, 131.4, 131.9, 132.8 (d, <sup>3</sup>J<sub>C-F</sub> = 7.8 Hz), 132.8 (d, <sup>3</sup>J<sub>C-F</sub> = 8.0 Hz), 135.1), Ar-CH], [(136.4 (d, <sup>4</sup>J<sub>C-F</sub> = 4.0 Hz), 136.4 (d, <sup>4</sup>J<sub>C-F</sub> = 4.0 Hz), 139.6, 139.7, 139.8, 140.1, 140.1, 140.3, 140.6, 140.7, 140.8), quarternary Ar-C] and 160.8 (d, <sup>1</sup>J<sub>C-F</sub> = 243.6 Hz, C–F); <sup>19</sup>F NMR (376 MHz, CDCl₃) δ ppm: -116.86 and -116.84; FTIR (neat) v<sub>max</sub> (cm⁻¹): 3304 (w, sp ≡C–H stretch), [3056, 3026 (w, Ar C–H stretch), [1603, 1577, 1510 (m, Ar C=C stretch)] and 1224 (m, Ar C–F stretch); UV/Vis (CH₂Cl₂) λ<sub>max</sub> (nm): 244 and 276 (log ε 4.87 and 4.28); Fluorescence (CH₂Cl₂, λ<sub>exc</sub> 376 nm) λ<sub>ems</sub> (nm): 413, 437 and 464; HRMS Calcd for C₄₄H₂₈F₂ [M]+: 594.2154, Found: 594.2146.

Expansion of 159 with Pendant 241: Synthesis of Dendrimer 242

Dendrimer 159 (80.0 mg, 0.06 mmol, 1.0 equiv.), pendant 241 (220.0 mg, 0.37 mmol, 6.0 equiv.), Pd(PPh₃)₂Cl₂ (8.6 mg, 0.012 mmol, 20 mol%), PPh₃ (6.4 mg, 0.024 mmol, 40 mol%), Cul (4.7 mg, 0.024 mmol, 40 mol%), Et₃N (2.4 mL) and anhydrous toluene (2.4 mL) were treated as described in General Procedure A. Purification by preparative TLC (SiO₂, hexane/CH₂Cl₂ = 7:3) afforded by-products 248 (32.0 mg, 15%) as white powder, 294 (28.1 mg, 26%) as yellow powder and 250 (11.0 mg, 8%) as yellow powder.
**Data for 248:**

TLC $R_f$ = 0.23 (hexane/CH$_2$Cl$_2$ = 7:3); melting point = > 300 °C; $^1$H NMR (400 MHz, CD$_2$Cl$_2$) δ ppm: 6.56-6.62 (m, 8H), 6.78-6.99 (m, 47H); Very poor solubility in many solvents, $^{13}$C NMR could not be obtained; $^{19}$F NMR (470 MHz, CD$_2$Cl$_2$) δ ppm: -117.60 and -117.57; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3081, 3059, 3028 (w, Ar C–H stretch)], [1604 (m), 1512 (s) (Ar C=C stretch)] and 1235 (s, Ar C–F stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 247, 275, 295, 315 and 337 (log $\varepsilon$ 5.03, 4.76, 4.49, 4.53 and 4.46); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 376 nm) $\lambda_{\text{ems}}$ (nm): 413, 437 and 462; ASAP-MS Calcd for C$_{88}$H$_{55}$F$_4$ [M+H]$^+$: 1187.4234, Found: 1187.4226.

**Data for 249 (mixture of two spots in TLC):**

TLC $R_f$ = 0.18 and 0.15 (hexane/CH$_2$Cl$_2$ = 7:3); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 6.07-6.14 (m, 3H), 6.23-6.26 (m, 2H) and 6.54-7.05 (m, 72H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: [(82.4, 89.0, 89.1, 89.5, 89.6), C≡C], [(113.9 (d, $^2$J$_{C-F}$ = 21.3 Hz), 119.6, 119.6, 119.7, 119.7, 120.2, 120.3, 121.8, 121.8, 125.2, 125.4, 125.4, 125.5, 125.6, 125.6, 125.7, 125.7, 126.6, 126.8, 126.8, 126.8, 126.9, 126.9, 127.0, 127.1, 127.2, 127.2, 127.3, 127.3, 127.3, 128.9, 129.1, 129.1, 129.9, 129.9, 129.9, 130.0, 130.1, 130.1, 130.1, 130.2, 131.2, 131.3, 131.3, 131.4, 131.7, 132.8, 132.8, 132.9, 132.9, 132.9, 133.0, 133.1, 134.2), Ar-CH], [(135.7, 136.4, 136.5, 136.5, 138.7, 138.7, 139.2, 139.3, 139.5, 139.6, 139.6, 139.6, 139.7, 139.7, 139.8, 139.8, 140.0, 140.1, 140.3, 140.3, 140.4, 140.4, 140.4, 140.5, 140.6, 140.7, 140.7, 140.8, 140.8, 140.9), quaternary Ar-C] and 160.8 (d, $^1$J$_{C-F}$ = 243.6 Hz, C–F); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3055, 3025 (w, Ar C–H stretch)], [1601, 1577, 1510 (m, Ar C=C stretch)], 1223 (m, Ar C=F stretch) and 1072 (m, Ar C=Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 249, 276 and 315 (log $\varepsilon$ 5.09, 4.83 and 4.44); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 330 nm) $\lambda_{\text{ems}}$ (nm): 367; MALDI-TOF-MS Calcd for C$_{122}$H$_{77}$Br$_3$F$_4$ [M+H]$^+$: 1820.4, Found: 1820.3.

**Data for 250:**

TLC $R_f$ = 0.09 (hexane/CH$_2$Cl$_2$ = 7:3); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 6.07-6.13 (m, 3H), 6.23-6.25 (m, 2H), 6.51-7.02 (m, 99H); Small amount of sample not sufficient to obtain $^{13}$C NMR; FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3055, 3025 (w, Ar C–H stretch)], [1602, 1577, 1510 (m, Ar C=C stretch)], 1223 (m, Ar C=F stretch) and 1072 (m, Ar C=Br stretch); UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 249, 276 and 315 (log $\varepsilon$ 5.09, 4.83 and 4.44); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 330 nm) $\lambda_{\text{ems}}$ (nm): 367; MALDI-TOF-MS Calcd for C$_{122}$H$_{77}$Br$_3$F$_4$ [M+H]$^+$: 1820.4, Found: 1820.3.
Experimental

1510 (m, Ar C=C stretch), 1223 (m, Ar C–F stretch) and 1072 (m, Ar C–Br stretch);
UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 247, 276 and 316 (log $\varepsilon$ 4.93, 4.72 and 4.40);
Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 336 nm) $\lambda_{\text{ems}}$ (nm): 371; MALDI-TOF-MS Calcd for C$_{166}$H$_{104}$Br$_2$F$_4$ [M]$^+$: 2334.6, Found: 2333.7.

1-Iodo-3-(2-phenylethynyl)benzene (258)
1,3-Diiodobenzene (5.1001 g, 15.5 mmol, 1.0 equiv.), phenylacetylene (1.7 mL, 15.5 mmol, 1.0 equiv.), Pd(PPh$_3$)$_2$Cl$_2$ (0.1085 g, 0.15 mmol, 1 mol%), CuI (0.0294 g, 0.15 mmol, 1 mol%) and Et$_3$N (125 mL) were treated as described in General Procedure A. Purification by flash column chromatography (SiO$_2$, hexane) afforded 258 (2.3156 g, 49%) as a yellow crystalline solid and by-product 127 (0.7374 g, 17%) as a white solid.

TLC $R_f$ = 0.48 (hexane); melting point = 49-50 °C (lit. 45-47 °C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 7.08 (t, 7.8 Hz, 1H, H-13), 7.35-7.38 (m, 3H, H-2/3/4), 7.50 (ddd, 0.8, 1.6 and 7.8 Hz, 2H, H-14), 7.53-7.55 (m, 2H, H-1/5), 7.67 (ddd, 0.8, 1.6 and 7.8 Hz, 2H, H-12) and 7.91 (t, 1.6 Hz, 1H, H-10); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 87.8, (C-8), 90.8 (C-7), 93.8 (C-11), 122.9 (C-7), 125.5 (C-6), 128.5 (C-2/4), 128.7 (C-3), 130.0 (C-13), 130.8 (C-14), 131.8 (C-1/5), 137.3 (C-12) and 140.3 (C-10); FTIR (neat) $\nu_{\text{max}}$ (cm$^{-1}$): [3078, 3056 (w, Ar C–H stretch)] and [1598, 1577, 1545 (m, Ar C=C stretch)]; GC/MS-EI [M]$^+$ m/z = 304 (100%), 305 (22%) and 306 (2%); HRMS Calcd for C$_{14}$H$_9$I [M]$^+$: 303.9743, Found: 303.9751.

Data collected matched the reported data, full NMR assignment made by the author.

4,4’-bis(2-Triisopropylsilylethynyl)benzil (260)
4,4’-Dibromobenzil (1.1040 g, 3.0 mmol, 1.0 equiv.), triisopropylsilylacetylene (1.4 mL, 6.6 mmol, 1.0 equiv.), Pd(PPh$_3$)$_2$Cl$_2$ (0.2106 g, 0.3 mmol, 10 mol%), PPh$_3$ (0.1572 g, 0.6 mmol, 20%), CuI (0.1143 g, 0.6 mmol, 20 mol%), Et$_3$N (24 mL) and anhydrous toluene (12 mL) were treated as described in General Procedure A for 4 h. Purification by flash column chromatography (SiO$_2$, hexane/EtOAc = 99:1) afforded 260 (0.1431 g, 84%) as a viscous yellow liquid.
**Experimental**

**TLC** 
*Rf* = 0.38 (hexane/EtOAc = 99:1); **1H NMR** (400 MHz, CDCl₃) δ ppm: 1.12-1.14 (m, 42H, –CH(CH₃)₃), 7.58 (d, 8.8 Hz, 4H, H-4/6/22/24) and 7.90 (d, 8.8 Hz, 4H, H-3/7/21/25); **13C NMR** (100 MHz, CDCl₃) δ ppm: 11.4 (–CH(CH₃)₃), 18.8 (–CH(CH₃)₃), 96.9 (C-9/27), 105.9 (C-8/26), 129.8 (C-3/7/21/25), 130.4 (C-5/23), 132.1 (C-2/20), 132.6 (C-4/6/22/24) and 193.4 (C-1/19); **FTIR** (neat) \( \nu \text{max} \) (cm⁻¹): [2941, 2890, 2864 (s, \text{sp}³ C–H stretch)], 2156 (w, C≡C stretch), 1671 (s, C=O stretch), [1598, 1556 (m, Ar C=C)], 1461 (m, Si–C stretch), 1384 (m, \text{sp}³ C–H bend) and 1207 (s, Si–C stretch); **ESI-MS** [M+Na]+ \( m/z \) = 593.5.

Data collected matched the reported data,²⁹ full NMR assignment made by the author.

**3,4-bis(4-(2-Triisopropylsilyl ethynyl)phenyl)-2,5-diphenylcyclopenta-2,4-dienone** (56)

Compound 260 (3.81 g, 6.7 mmol, 1.0 equiv.), 1,3-diphenyl-2-propanone (1.54 g, 7.4 mmol, 1.0 equiv.) and EtOH (105 mL) as well as KOH (0.30 g, 5.4 mmol) and EtOH (20 mL) were treated as described in General Procedure D. Purification by flash column chromatography (SiO₂, hexane/EtOAc = 99:1) to obtain mixture of product and inseparable by-products 56 (4.12 g, 83%).

**TLC** 
*Rf* = 0.40 (hexane/EtOAc = 20:1); **1H NMR** (400 MHz, CDCl₃) δ ppm: 1.12 (s, 42H, H-18/19/20/21/22/23/24/25/26/36/37/38/39/40/41/42/43/44), 6.87 (d, 8.6 Hz, 4H, H-11/15/29/33), 7.19 (m, 4H, H-5/7/48/50), 7.23-7.26 (m, 6H, H-4/6/8/47/49/51) and 7.29 (d, 8.6 Hz, 4H, H-12/14/30/32); **13C NMR** (100 MHz, CDCl₃) δ ppm: 11.5 (C-18/21/24/36/39/42), 18.8 (C-19/20/22/23/25/26/37/38/40/41/43/44), 92.5 (C-17/35), 106.8 (C-16/34), 123.9 (C-10/28), 126.1 (C-2/48), 127.8 (C-6/49), 128.3 (C-4/8/47/51), 129.4 (C-11/15/29/33), 130.3 (C-5/7/48/50), 130.6 (C-3/46), 131.9 (C-12/14/30/32), 132.9 (C-13/31), 153.4 (C-9/27) and 199.8 (C-1); **FTIR** (neat) \( \nu \text{max} \) (cm⁻¹): [3079, 3053, 3034 (w, Ar C–H stretch)], [2941, 2890, 2863 (s, \text{sp}³ C–H stretch)], 2152 (m, C≡C stretch), 1710 (s, C=O stretch), [1602, 1489 (m, Ar C=C stretch)], 1444 (w, Si–C stretch) and 1356 (m, \text{sp}³ C–H bend); **APCI-MS** [M+H]+ \( m/z \) = 745; **HRMS**
Calcd for $\text{C}_{51}\text{H}_{62}\text{OSi}_2 [\text{M}+\text{H}]^+ : 745.4261$, Found: 745.4261.

Data collected matched the reported data,\textsuperscript{29} full NMR assignment made by the author.

6.12 Other Work

*Synthesis of Cu(I)-complex with Pyridyl-containing Dendrimer*

Dendrimer 165 (26.0 mg, 0.02 mmol) and CuI (3.8 mg, 0.02 mmol) was dissolved in CH$_2$Cl$_2$ (1.5 mL). The cloudy mixture was stirred overnight at room temperature. The resulting clear solution was concentrated to afford mixture of unreacted dendrimer 165, complex 261 and complex 262 (25.0 mg, 84%) as yellow powders.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm:
5.48 ($d$, 6.9 Hz, 1H), 6.27-7.07 ($m$, 44H), 7.50 ($d$, 7.2 Hz, 1H), 7.64 ($td$, 1.3 and 7.6 Hz, 1H) and 8.67 ($d$, 4.9 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 119.7, 119.8, 119.9, 120.9, 120.9, 121.0, 125.0, 125.2, 125.5, 125.6, 125.7, 125.7, 125.7, 126.2, 126.7, 126.7, 126.8, 126.8, 127.0, 127.0, 127.1, 127.1, 127.2, 127.2, 127.3, 127.4, 127.4, 127.6, 129.4, 129.6, 129.6, 129.7, 129.8, 129.9, 130.0, 130.1, 130.1, 130.2, 130.2, 131.9, 132.4, 132.7, 132.8, 132.8, 132.8, 132.9, 133.0, 133.0, 133.1, 133.5, 135.8, 135.8, 138.6, 138.6, 138.7, 138.7, 139.0, 139.3, 139.5, 139.6, 140.0, 140.0, 140.2, 140.47, 141.2 and 160.2; UV/Vis (CH$_2$Cl$_2$) $\lambda_{\text{max}}$ (nm): 247 and 380 (log $\varepsilon$ 4.92 and 4.54); Fluorescence (CH$_2$Cl$_2$, $\lambda_{\text{exc}}$ 365 nm) $\lambda_{\text{ems}}$ (nm): 414, 438 and 469; ESI-MS Dendrimer 165 [M+Cu]$^+$ or Complex 261 [M–I]$^+$ $m/z = 1370.3$.

*Synthesis of Glycodendrimer (265)*

Lactose-containing monoadduct 264 (100 mg, 0.11 mmol, 1.0 equiv.), 142 (91 mg, 0.17 mmol, 1.5 equiv.) and anhydrous o-xylene (1 mL) were treated as described in General Procedure E at 175 °C for 5 d. Most of the impurities were separated by flash column chromatography (SiO$_2$, hexane/EtOAc, 6:1 to 1:1) to give impure dark yellow powder of glycodendrimer 265 (113 mg, 72%).
**Experimental**

\[ R_f = 0.45 \text{ (hexane/EtOAc} = 7:3); \]  

\[ ^1H \text{ NMR} \text{ (400 MHz, CDCl}_3 \text{)} \delta \text{ppm: 1.86 (s, 4H), 1.96 (s, 5H), 2.04-2.09 (m, 19H), 2.15 (s, 5H), 3.33 (s, 3H), 3.47-3.50 (m, 2H), 3.66-3.68 (m, 2H), 3.88-3.98 (m, 4H), 4.06-4.17 (m, 5H), 4.45-4.53 (m, 3H), 4.95-5.00 (m, 3H), 5.10-5.15 (m, 1H), 5.35-5.36 (m, 2H), 5.39-5.41 (m, 2H), 5.82-5.85 (m, 1H), 6.61-6.70 (m, 6H), 6.83-6.85 (m, 2H), 6.94-6.97 (m, 3H), 7.02 (d, 8.0 Hz, 3H), 7.07-7.11 (m, 5H), 7.16-7.18 (m, 4H), 7.28-7.29 (m, 1H), 7.34 (s, 1H), 7.59 (s, 1H) and 7.77 (s, 1H); ESI-MS \ [M+Na]^+ m/z = 1426. \]
References

References


(64) Minard-Basquin, C.; Weil, T.; Hohner, A.; Rädler, J. O.; Müllen, K. J. Am. Chem. 296
References

Soc. 2003, 125, 5832–5838.
References

(142) Mathematica; Wolfram Research, Inc.: Champaign, IL, 2014.
Appendix A. Mass Spectra of Dendrimers

Pentaaryl Dendrimers

Penta-H-Br-Br (150):

Penta-H-F-F (151):
Appendix A. Mass Spectra

Penta-OMEM-Br-Br (152)

Molecular formula: C_{70}H_{56}Br_{12}Na_{32}Ha
Resolution: 5000 at 50%

Theoretical [M+Na]⁺

Observed Data

Penta-OH-Br-Br (153)

Molecular formula: C_{68}H_{42}Br_{12}Na_{32}Ha
Resolution: 5000 at 50%

Theoretical [M+Na]⁺

Observed Data
Appendix A. Mass Spectra

Penta-OH-F-F (154)

Theoretical [M]^+

Observed Data

Penta-H-Br-F (157)

Theoretical [M+Na]^+

Observed Data
Appendix A. Mass Spectra

Penta-OH-Br-F (158)

Hexaaryl Dendrimers
Hexa-H-Phenyl-Br-Br (159)
Appendix A. Mass Spectra

Hexa-H-Phenyl-F-F (160)

Hexa-OTBDMS-Phenyl-Br-Br (161)
Appendix A. Mass Spectra

Hexa-OTBDMS-Phenyl-F-F (162)

Molecular formula: C92H145NO13S. Resolution: 5000 at 50%.

Theoretical [M+Na]+

Observed Data

Hexa-OH-Phenyl-Br-Br (163)

Molecular formula: C13H155NO12S. Resolution: 5000 at 50%.

Theoretical [M+Na]+

Observed Data
Appendix A. Mass Spectra

Hexa-(OCH$_2$F)-Phenyl-Br-Br (174)

[Mass spectrum diagram]

Theoretical [M+Na$^+$]

Experiment: 357 (approx.) m/z 357
Calc: 357.2132 (exact)
Calculated: 357.2138 (exact)

Hexa-[(OCH$_2$)-Phenyl-Br-Br]$_2$ (175)

[Mass spectrum diagram]

Theoretical M$^+$

Experiment: 714.60 (approx.) m/z 714.60
Calc: 714.601 (exact)
Calculated: 714.601 (exact)

Observed Data (very weak)
Appendix A. Mass Spectra

Hexa-OH-Phenyl-F-F (164)

Molecular formula: C7H8O5F4Ph

Theoretical [M+Na]⁺

Observed Data

Hexa-H-(2-Pyridyl)-Br-Br (165)

Molecular formula: C10H7Br3NPh

Theoretical [M+H]⁺

Observed Data
Hexa-OMEM-(2-Pyridyl)-Br-Br (166)

Hexa-OH-(2-Pyridyl)-Br-Br (167)
Hexa-H-(4-Fluorophenyl)-Br-Br (168)

Hexa-H-(4-Fluorophenyl)-F-F (169)
Appendix A. Mass Spectra

Hexa-OH-(4-Fluorophenyl)-Br-Br (170)

Hexa-H-(2-Fluorophenyl)-Br-Br (171)
Hexa-H-(2-Fluorophenyl)-F-F (172)

Theoretical $[M+Na]^+$

Observed Data

Hexa-OH-(2-Fluorophenyl)-Br-Br (173)

Observe Data (very weak)

Theoretical M$^+$

Acquired: 09:33 BST, March 23, 2015
Processed with SPIA 2.4.1
Software: SPIA B (DARWIN) 2.4.1 (DARWIN)
Appendix A. Mass Spectra

Hexa-H-Phenyl-Br-F (184)

Hexa-OTBDMS-Phenyl-Br-F (185)
Hexa-OH-Phenyl-Br-F (186)

Hexa-H-(4-Fluorophenyl)-Br-F (187)
Hexa-OH-(4-Fluorophenyl)-Br-F (188)

Hexa-H-(2-Fluorophenyl)-Br-F (189)
Hexa-OH-(2-Fluorophenyl)-Br-F (190)

Ester of Pentaaryl Dendrimers
Penta-OAAux -Br-Br (221)
Appendix A. Mass Spectra

Penta-OAAux -F-F (222)

![Mass Spectra of Penta-OAAux -F-F (222)]

Penta-OAAux-Br-F (223)

![Mass Spectra of Penta-OAAux-Br-F (223)]
Appendix A. Mass Spectra

Penta-OCAux-Br-Br (224)

Theoretical [M+H]⁺

Observed Data

Penta-OCAux-F-F (225)

Theoretical [M+Na]⁺

Observed Data
Ester of Hexaaryl Dendrimers

Hexa-OAAux-Phenyl-Br-Br (226)

Hexa-OAAux-Phenyl-F-F (227)
Appendix A. Mass Spectra

Hexa-OAAux-Phenyl-Br-F (228)

Hexa-OAAux-(4-Fluorophenyl)-Br-Br (229)
Hexa-OAAux-(4-Fluorophenyl)-Br-F (230)

[Mass Spectra Diagram]

Hexa-OAAux-(2-Fluorophenyl)-Br-Br (231)

[Mass Spectra Diagram]
Appendix A. Mass Spectra

Hexa-OAAux-(2-Fluorophenyl)-Br-F (232)

Ester of Hexaaryl Dendrimer Monoadducts

Hexa-OAAux-(4-Fluorophenyl)-Br (233)
Hexa-OAAux-(2-Fluorophenyl)-Br (234)

Dendrimer Expansions
Expansion Unit 247
Appendix A. Mass Spectra

Monocoupled by-product 248

Expanded Dendrimer 249
Expanded Dendrimer 250

Penta-OVal-Br-Br (236)
Penta-O\textsubscript{Val}-F-F (237)

Other Work

Cu(I) mixture with dendrimer 165
Glycodendrimer (265)
Appendix B. BIRD HSQC Spectra of Dendrimers 170 and 173

*Hexa-OH-(4-Fluorophenyl)-Br-Br (170)*
## Appendix B. BIRD HSQC Spectra

<table>
<thead>
<tr>
<th>No</th>
<th>$^1$H Chemical shift (δ, ppm)</th>
<th>$^{13}$C Chemical shift (δ, ppm)</th>
<th>$J_{HF}$ (Hz)</th>
<th>$J_{CF}$ (Hz)</th>
<th>Position relative to fluorine</th>
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Appendix B. BIRD HSQC Spectra

Hexa-OH-(2-Fluorophenyl)-Br-Br (173)
### Appendix B. BIRD HSQC Spectra

![Diagram of BIRD HSQC Spectra](image)

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<thead>
<tr>
<th>No</th>
<th>H Chemical shift (δ, ppm)</th>
<th>C Chemical shift (δ, ppm)</th>
<th>$J_{HF}$ (Hz)</th>
<th>$J_{CF}$ (Hz)</th>
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<td>4.9</td>
<td>4.0</td>
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</tbody>
</table>

* One of the cross peaks that belongs to peak 3 overlapped with peak 2 and the coupling constant values for peak 3 could not be determined. Position was determined based on the trend of the peaks in this region and the equivalent of this peak in dendrimer 171.

* It was difficult to determine the $J_{HF}$ value for the peaks belonging to the proton para to fluorine because the coupling constant value was small (0.3-1.5 Hz). The $J_{CF}$ values of these carbons were similar to the $J_{CF}$ values for the carbons on the meta position. However, since the $J_{HF}$ on the meta position was observable, the protons and carbons on the para position could be determined by elimination based on the $J_{CF}$ values.

* One of the cross peaks that belongs to peak 15 overlapped with noise and the coupling constant values could not be determined. Position was determined based on the trend of the peaks in this region and the equivalent of this peak in dendrimer 171.
Appendix C. Variable Temperature NMR Spectra

**VT $^{19}$F NMR of Dendrimer Hexa-H-(2-Fluorophenyl)-Br-Br 189**

470 MHz, CDCl$_3$
Appendix C. VT NMR Spectra of Dendrimers

$^{19}$F NMR of Dendrimer Hexa-OAAux-(2-Fluorophenyl)-Br-Br

470 MHz, CDCl$_3$
Appendix C. VT NMR Spectra of Dendrimers

VT\textsuperscript{13}C NMR of Dendrimer Penta-OA\textsubscript{Aux}-Br-Br 223

125 MHz, DMF-\textit{d}\textsubscript{7} (1,4-dioxane as internal standard)
Appendix C. VT NMR Spectra of Dendrimers
Appendix C. VT NMR Spectra of Dendrimers
Appendix C. VT NMR Spectra of Dendrimers
Appendix D. Lineshape Fitting Results of Dendrimers 171 and 173

Comparison between experimental and lineshape fitting results for dendrimer 171

![Hexa-H-(2-Fluorophenyl)-Br-Br 171](image)

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>Experimental</th>
<th>Lineshape Fitting</th>
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<tr>
<td>323</td>
<td>[Graph]</td>
<td>[Graph]</td>
</tr>
<tr>
<td>313</td>
<td>[Graph]</td>
<td>[Graph]</td>
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<tr>
<td>293</td>
<td>[Graph]</td>
<td>[Graph]</td>
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<tr>
<td>283</td>
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<td>[Graph]</td>
<td>[Graph]</td>
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<tr>
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### Peak area obtained from lineshape fitting for dendrimer 171

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<th>Temp (K)</th>
<th>Peaks and Peaks Area</th>
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<tr>
<td>263</td>
<td>165.850 22.479 159.845 155.818 153.600 166.455 184.242 149.980</td>
</tr>
<tr>
<td>273</td>
<td>83.227 12.938 80.074 77.229 77.523 183.156 75.088</td>
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<tr>
<td>283</td>
<td>108.455 18.913 107.952 102.827 107.108 274.452 102.745</td>
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<tr>
<td>293</td>
<td>125.546 24.933 128.972 121.104 128.925 146.281 161.091 120.529</td>
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<tr>
<td>303</td>
<td>89.667 19.474 94.033 87.883 92.983 110.247 118.359 84.625</td>
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<tr>
<td>313</td>
<td>138.153 32.014 146.884 146.293 146.893 189.807 135.128</td>
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<tr>
<td>323</td>
<td>184.409 45.732 199.835 182.043 198.263 229.046 257.864 180.674</td>
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* Peaks 6 and 7 overlap at these temperatures and could not be resolved.
In order to prove that the ratio between peaks 3/5 and 4/8 are the ones that remain closest to 1:1 ratio at all temperatures, comparison of the peaks area were carried out using peaks 3, 4, 5 and 8 as reference peaks. Due to the overlap between peaks 6 and 7 at 273 and 283 K, the ratio between these peaks and the rest of the peaks at these temperatures was not determined.

**Ratio of peaks using peak 3 as reference**

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<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<td><strong>1.00</strong></td>
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**Ratio of peaks using peak 4 as reference**

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Comparison between experimental and lineshape fitting results for dendrimer 173

Hexa-OH-(2-Fluorophenyl)-Br-Br

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Peak area obtained from lineshape fitting for dendrimer 173

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340
### Ratio of peaks using peak 3 as reference

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### Ratio of peaks using peak 4 as reference

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<td>1.00</td>
<td>0.96</td>
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Appendix E. Complete Lineshape Analysis of VT $^{13}$C NMR Spectra of 223

Complete lineshape analysis of the VT $^{13}$C NMR spectra (125 MHz, DMF-$d_7$) of dendrimer 223 was performed using \textit{dnnr} module in Bruker TopSpin 3.1 software, to the set of peaks at 127.8-128.0 ppm. The fitting was performed on the intensities, chemical shifts and rate constants of the exchanging peaks using Simplex iterations.

<table>
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<th>Simulation</th>
<th>Temperatures/ Rate Constants</th>
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<tr>
<td></td>
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<td>3648.46 s$^{-1}$</td>
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<td></td>
<td></td>
<td>363 K</td>
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<tr>
<td></td>
<td></td>
<td>1763.30 s$^{-1}$</td>
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<td></td>
<td></td>
<td>353 K</td>
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<tr>
<td></td>
<td></td>
<td>990.12 s$^{-1}$</td>
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<tr>
<td></td>
<td></td>
<td>343 K</td>
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<tr>
<td></td>
<td></td>
<td>538.74 s$^{-1}$</td>
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<td>333 K</td>
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<td>259.76 s$^{-1}$</td>
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<td>323 K</td>
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<td>293 K</td>
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<td>10.13 s$^{-1}$</td>
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Appendix F. Kinetic and Thermodynamic Measurements of Various Dendrimers

2D EXSY (Varying Mixing Time) Processing

2D EXSY (Single Mixing Time) and 1D $^{19}$F NMR Processing

Fundamental Constants

Gas constant: $R = 8.3144 \text{ J K}^{-1} \text{ mol}^{-1}$

Planck constant: $h = 6.626 \times 10^{-34} \text{ J s}$

Boltzmann constant: $k_B = 1.38 \times 10^{-23} \text{ J K}^{-1}$

Equations

Extracting $k$ from EXSY with varying mixing times:

$I_{AA}(t_m) = X_A e^{-Rt_m} [X_A + X_B e^{-k t_m}] M^0$  
Eq. (4)

$I_{BB}(t_m) = X_B e^{-Rt_m} [X_B + X_A e^{-k t_m}] M^0$  
Eq. (5)

$I_{AB}(t_m) = I_{BA}(t_m) = X_A X_B e^{-Rt_m} [1 - e^{-k t_m}] M^0$  
Eq. (6)

Extracting $k$ from EXSY with a single mixing time:

$k = \frac{1}{t_m} \ln \frac{r + 1}{r - 1}$  
Eq. (8)

$r = \frac{4 (X_A X_B) (I_{AA} + I_{BB})}{(I_{AB} + I_{BA})} - (X_A - X_B)^2$  
Eq. (9)

Obtaining rate constants for individual processes:

$k = k_f + k_r$  
Eq. (10)  
$k_f = X_B k$  
Eq. (12)

$k_f X_A = k_r X_B$  
Eq. (11)  
$k_r = X_A k$  
Eq. (13)
Appendix F. Kinetics and Thermodynamics of Dendrimers

**Penta-OAAux-Br-Br (223)**

Free energy of activation and half-lives obtained from rate constants:

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>k (s⁻¹)</th>
<th>∆G° (kJ mol⁻¹)</th>
<th>t¹/₂ (ms)</th>
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<tr>
<td>283</td>
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<tr>
<td>373</td>
<td>3648.46</td>
<td>66.61</td>
<td>0.19</td>
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</table>

**Eyring Plot**

\[ y = -7525.82 \times 10^{-10} x + 22.2932 \]

\[ R^2 = 0.990155 \]

\[ \Delta H^\ddagger = 62.57 \text{ kJ mol}^{-1} \]

\[ \Delta S^\ddagger = -12.19 \text{ J mol}^{-1} \]

**Arrhenius Plot**

\[ y = -7849.85 x + 29.0779 \]

\[ R^2 = 0.990718 \]

\[ E_a = 65.27 \text{ kJ mol}^{-1} \]

\[ A = 4.25 \times 10^{12} \text{ s}^{-1} \]
**Hexa-H-(4-Fluorophenyl)-Br-Br (168)**

Energy diagram, rate constants, free energies of activation and half-lives:

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<th>$k_{12}$ (s⁻¹)</th>
<th>$k_{21}$ (s⁻¹)</th>
<th>$\Delta G^e_{12}$ (kJ mol⁻¹)</th>
<th>$\Delta G^r_{12}$ (J mol⁻¹)</th>
<th>$t_{1/2-(12)}$ (s)</th>
<th>$\Delta G^e_{21}$ (kJ mol⁻¹)</th>
<th>$\Delta G^r_{21}$ (J mol⁻¹)</th>
<th>$t_{1/2-(21)}$ (s)</th>
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**Forward Process**

**Eyring Plot**

\[ y = -9338.04x + 24.6636 \]

\[ R^2 = 0.991418 \]

\[ \Delta H^\circ = 77.64 \text{ kJ mol}^{-1} \]

\[ \Delta S^\circ = 7.52 \text{ J mol}^{-1} \]

**Arrhenius Plot**

\[ y = -9634.48x + 31.3569 \]

\[ R^2 = 0.991876 \]

\[ E_a = 80.10 \text{ kJ mol}^{-1} \]

\[ A = 4.15 \times 10^{13} \text{ s}^{-1} \]

**Reverse Process**

**Eyring Plot**

\[ y = -9399.89x + 24.6687 \]

\[ R^2 = 0.991548 \]

\[ \Delta H^\circ = 78.15 \text{ kJ mol}^{-1} \]

\[ \Delta S^\circ = 7.56 \text{ J mol}^{-1} \]

**Arrhenius Plot**

\[ y = -9696.33x + 31.3619 \]

\[ R^2 = 0.991992 \]

\[ E_a = 80.62 \text{ kJ mol}^{-1} \]

\[ A = 4.17 \times 10^{13} \text{ s}^{-1} \]
Hexa-H-(2-Fluorophenyl)-Br-Br (171)

Appendix F. Kinetics and Thermodynamics of Dendrimers

347
Energy diagram, rate constants, free energies of activation and half-lives:

![Energy diagram](image)

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<thead>
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<th>Exchange System</th>
<th>Temp (K)</th>
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<th>$k_r$ (s$^{-1}$)</th>
<th>$ΔG^e_{f}$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-\text{eq}}$ (s)</th>
<th>$ΔG_r$ (J mol$^{-1}$)</th>
<th>$ΔG^e_{r}$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-\text{eq}}$ (s)</th>
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</table>
Appendix F. Kinetics and Thermodynamics of Dendrimers

**Hexa-H-(4-Fluorophenyl)-Br-F (187)**

![Chemical structure of Hexa-H-(4-Fluorophenyl)-Br-F (187)](image)

![NMR spectra for Hexa-H-(4-Fluorophenyl)-Br-F (187)](image)
Energy diagram, rate constants, free energies of activation and half-lives:

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2}$(0) (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_f^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2}(r)$ (s)</th>
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Appendix F. Kinetics and Thermodynamics of Dendrimers

*Hexa-H-(2-Fluorophenyl)-Br-F (189)*

![Diagram of Hexa-H-(2-Fluorophenyl)-Br-F (189)](image-url)
Energy diagram, rate constants, free energies of activation and half-lives:
Appendix F. Kinetics and Thermodynamics of Dendrimers

**Hexa-OAAux-(4-Fluorophenyl)-Br-Br (229)**

![Chemical structure of Hexa-OAAux-(4-Fluorophenyl)-Br-Br (229)](image)

![NMR spectra](image)
Energy diagram, rate constants, free energies of activation and half-lives:

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^\ddagger$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2,f}$ (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_r^\ddagger$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2,r}$ (s)</th>
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<tr>
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Appendix F. Kinetics and Thermodynamics of Dendrimers

Hexa-OAAux-(4-Fluorophenyl)-Br-F (230)
Energy diagram, rate constants, free energies of activation and half-lives:

<table>
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<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_i$ (s$^{-1}$)</th>
<th>$\Delta G_r^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_r^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-r}$ (s)</th>
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</thead>
<tbody>
<tr>
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<td>0.085</td>
<td>0.061</td>
<td>79.09</td>
<td>8.15</td>
<td>839.28</td>
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<tr>
<td>2 $\leftrightarrow$ 5</td>
<td>0.082</td>
<td>0.080</td>
<td>79.17</td>
<td>8.42</td>
<td>70.05</td>
<td>79.24</td>
<td>8.66</td>
</tr>
<tr>
<td>5 $\leftrightarrow$ 6</td>
<td>0.058</td>
<td>0.057</td>
<td>80.05</td>
<td>11.98</td>
<td>25.55</td>
<td>80.07</td>
<td>12.11</td>
</tr>
<tr>
<td>6 $\leftrightarrow$ 8</td>
<td>0.075</td>
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<td>79.41</td>
<td>9.28</td>
<td>790.92</td>
<td>80.20</td>
<td>12.77</td>
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</table>
Hexa-OAAux-(2-Fluorophenyl)-Br-Br (231)
Appendix F. Kinetics and Thermodynamics of Dendrimers
Appendix F. Kinetics and Thermodynamics of Dendrimers
Energy diagrams:

EXSY Square ‘1’

EXSY Square ‘2’

EXSY Square ‘3’

EXSY Square ‘7’
Rate constants, free energies of activation and half-lives:

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s⁻¹)</th>
<th>$k_r$ (s⁻¹)</th>
<th>$\Delta G_f^\neq$ (kJ mol⁻¹)</th>
<th>$t_{1/2(f)}$ (s)</th>
<th>$\Delta G_r$ (J mol⁻¹)</th>
<th>$\Delta G_r^\neq$ (kJ mol⁻¹)</th>
<th>$t_{1/2(r)}$ (s)</th>
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<tbody>
<tr>
<td>1 ⇌ 6</td>
<td>0.110</td>
<td>0.047</td>
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<td>6.32</td>
<td>2103.80</td>
<td>80.56</td>
<td>14.77</td>
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<tr>
<td>6 ⇌ 9</td>
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<td>4.30</td>
<td>1390.55</td>
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<tr>
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<td>79.17</td>
<td>8.42</td>
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<td>0.036</td>
<td>80.94</td>
<td>17.17</td>
<td>283.18</td>
<td>81.22</td>
<td>19.25</td>
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<tr>
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<td>0.080</td>
<td>78.26</td>
<td>5.83</td>
<td>992.60</td>
<td>79.25</td>
<td>8.70</td>
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<td>10 ⇌ 13</td>
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<td>0.099</td>
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<td>-930.09</td>
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Appendix F. Kinetics and Thermodynamics of Dendrimers

Hexa-OAAux-(2-Fluorophenyl)-Br-F (232)

EXSY Square '1'
EXSY Square '3'
EXSY Square '5'
EXSY Square '13'

EXSY Square '2'
EXSY Square '4'
EXSY Square '6'
EXSY Square '14'
Appendix F. Kinetics and Thermodynamics of Dendrimers
Energy diagrams:
Rate constants, free energies of activation and half-lives:

<table>
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<th>EXSY Squares</th>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^o$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(f)}$ (s)</th>
<th>$\Delta G_r^o$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(r)}$ (s)</th>
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<td>1 $\Rightarrow$ 11</td>
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<td>80.07</td>
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<td>606.45</td>
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<td>5.76</td>
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<td>0.041</td>
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<td>0.040</td>
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<td>36.98</td>
<td>80.96</td>
<td>17.31</td>
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<td>80.62</td>
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<td>3462.39</td>
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<td>0.111</td>
<td>78.69</td>
<td>6.94</td>
<td>-263.11</td>
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<td>7.03</td>
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<td>80.08</td>
<td>12.16</td>
<td>-2340.80</td>
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<td>4.73</td>
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<td>4.72</td>
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<td>80.59</td>
<td>14.92</td>
<td>-2386.13</td>
<td>78.20</td>
<td>5.70</td>
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</table>
Appendix F. Kinetics and Thermodynamics of Dendrimers

MonoHexa-OAAux-(4-Fluorophenyl)-Br (233)
Energy diagram, rate constants, free energies of activation and half-lives:

\[
\begin{array}{cccccccc}
\text{Exchange System} & k_f \ (s^{-1}) & k_r \ (s^{-1}) & \Delta G_f^0 \ (kJ \ mol^{-1}) & t_{1/2-(f)} \ (s) & \Delta G_r \ (J \ mol^{-1}) & \Delta G_r^0 \ (kJ \ mol^{-1}) & t_{1/2-(r)} \ (s) \\
\text{a} \rightleftharpoons \text{b} \ (3 \rightleftharpoons 4) & 0.254 & 0.259 & 76.38 & 2.73 & -47.70 & 76.33 & 2.67 \\
\end{array}
\]
Appendix F. Kinetics and Thermodynamics of Dendrimers

**MonoHexa-H-(2-Fluorophenyl)-Br (182)**
Energy diagram, rate constants, free energies of activation and half-lives:

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_r$ (s$^{-1}$)</th>
<th>$\Delta G_f^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-f}$ (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_r^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2-r}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1/3 \neq 2/4$</td>
<td>0.253</td>
<td>0.213</td>
<td>76.39</td>
<td>2.74</td>
<td>425.33</td>
<td>76.81</td>
<td>3.25</td>
</tr>
</tbody>
</table>
Appendix F. Kinetics and Thermodynamics of Dendrimers

MonoHexa-OAAux-(2-Fluorophenyl)-Br (234)
Energy diagram, rate constants, free energies of activation and half-lives:

<table>
<thead>
<tr>
<th>Exchange System</th>
<th>$k_f$ (s$^{-1}$)</th>
<th>$k_i$ (s$^{-1}$)</th>
<th>$\Delta G_f^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(\alpha)}$ (s)</th>
<th>$\Delta G_r$ (kJ mol$^{-1}$)</th>
<th>$\Delta G_r^0$ (kJ mol$^{-1}$)</th>
<th>$t_{1/2(\alpha)}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 → 7</td>
<td>0.257</td>
<td>0.229</td>
<td>76.35</td>
<td>2.70</td>
<td>291.04</td>
<td>76.64</td>
<td>3.03</td>
</tr>
<tr>
<td>6 → 8</td>
<td>0.248</td>
<td>0.226</td>
<td>76.44</td>
<td>2.80</td>
<td>223.45</td>
<td>76.67</td>
<td>3.06</td>
</tr>
</tbody>
</table>
Appendix G. $^{13}$C NMR Spectra of Some Dendrimers

Hexa-H-(2-Pyridyl)-Br-Br (165)

Hexa-OMEM-(2-Pyridyl)-Br-Br (166)
Appendix G. $^{13}$C NMR Spectra

Hexa-H-(2-Fluorophenyl)-Br-Br (171)

Hexa-H-(2-Fluorophenyl)-F-F (172)
Appendix G. \( ^{13} \text{C} \) NMR Spectra

Hexa-OH-(2-Fluorophenyl)-Br-Br (173)

Hexa-H-(2-Fluorophenyl)-Br-F (189)
Appendix G. $^{13}$C NMR Spectra

Hexa-OH-(2-Fluorophenyl)-Br-F (190)

Hexa-OAAux-(2-Fluorophenyl)-Br-Br (231)
Appendix G. $^{13}$C NMR Spectra

Hexa-OAAux-(2-Fluorophenyl)-Br-F (232)